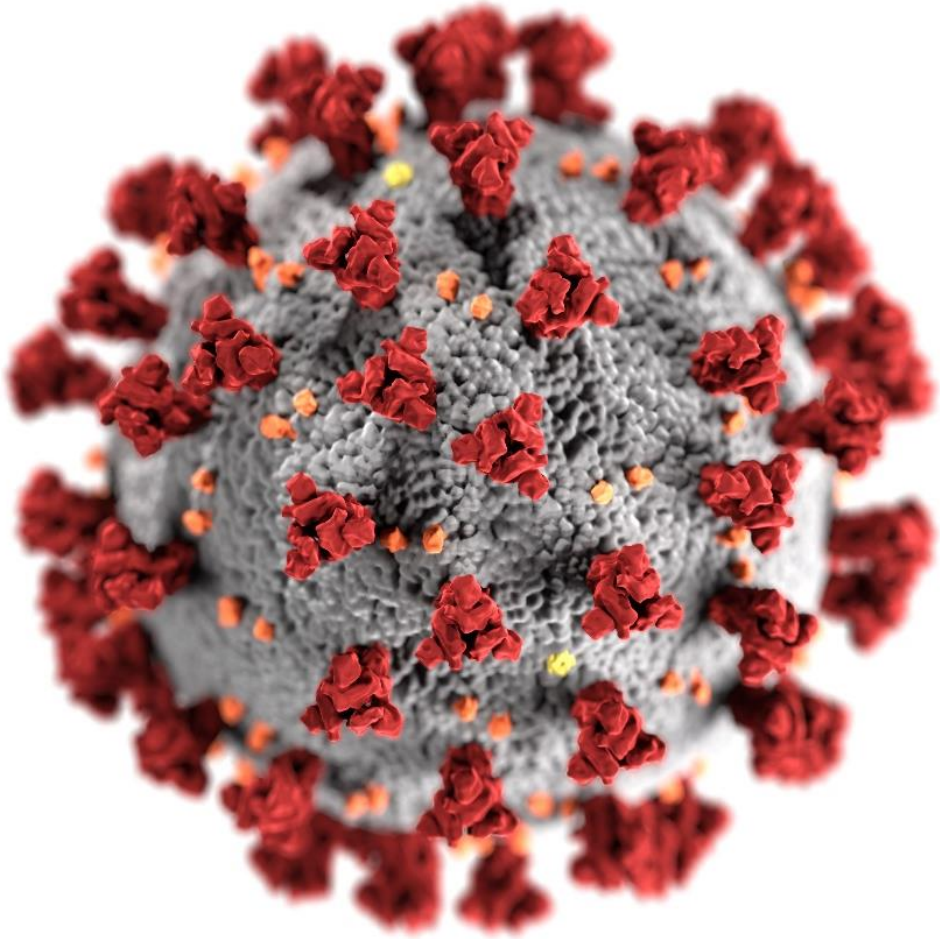
Updates to the Evidence to Recommendation Framework:

Pfizer-BioNTech and Moderna COVID-19 vaccine booster doses



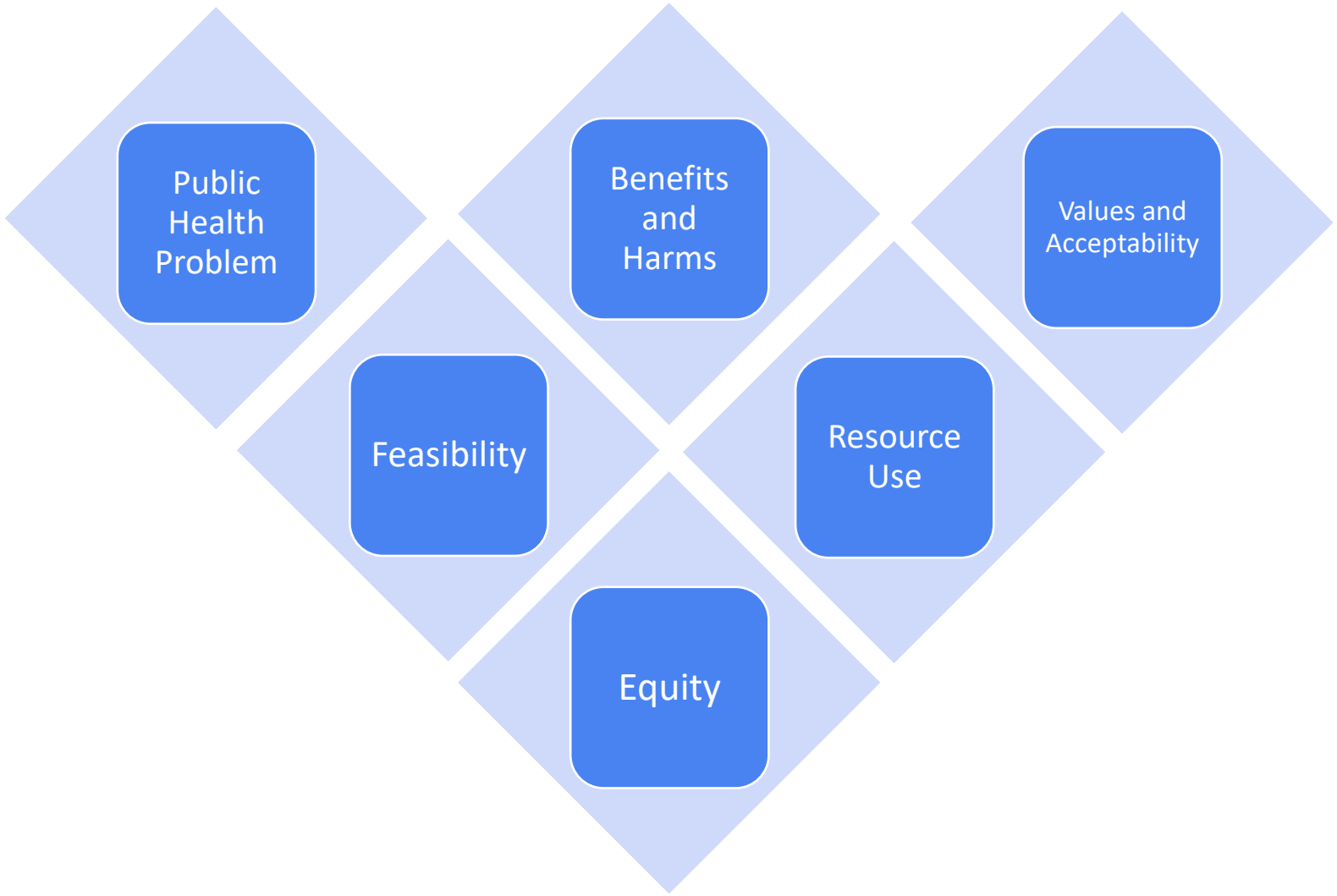
Sara Oliver, MD, MSPH

ACIP Meeting

November 19, 2021

cdc.gov/coronavirus

Evidence to Recommendations (EtR) Framework



Evidence to Recommendations (EtR) Framework

- Previous presentations/discussions for booster doses of COVID-19 vaccines

September 23rd:

COVID-19 vaccine booster doses: Benefit/risk discussion

Evidence to Recommendation Framework: Booster doses of Pfizer-BioNTech COVID-19 vaccine

VOTE: Pfizer-BioNTech COVID-19 booster doses

https://www.cdc.gov/vaccines/acip/meetings/slides-2021-09-22-23.html

October 21st:

National Institutes of Health: Mix and Match booster study

Evidence to Recommendation Framework: Booster doses of Moderna & Janssen COVID-19 vaccines

VOTE: Moderna & Janssen COVID-19 booster doses (including heterologous boosting)

https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html

COVID-19 vaccine booster dose in persons who received a Janssen COVID-19 vaccine primary dose

- Persons aged ≥18 years who received primary vaccination with Janssen COVID-19 vaccine **should** receive a single COVID-19 vaccine booster dose at least 2 months later

- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

COVID-19 vaccine booster dose in persons who completed an mRNA primary series

Persons who <u>should</u> receive a COVID-19 booster dose

- Aged ≥65 years
- Aged ≥18 years and reside in long-term care settings
- Aged 50-64 years with certain underlying medical conditions

Persons who <u>may</u> receive a COVID-19 booster dose, based on individual benefits and risks

- Aged 18-49 years with certain underlying medical conditions*
- Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting

- Booster dose administered at least 6 months after completion of primary series
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

* Includes pregnant people

COVID-19 vaccine booster dose in persons who completed an mRNA primary series

Persons who <u>should</u> receive a COVID-19 booster dose

- Aged ≥65 years
- Aged ≥18 years and reside in long-term care settings
- Aged 50-64 years with certain underlying medical conditions

Persons who <u>may</u> receive a COVID-19 booster dose, based on individual benefits and risks

- Aged 18-49 years with certain underlying medical conditions*
- Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting

- Booster dose administered at least 6 months after completion of primary series
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

* Includes pregnant people

Policy Question

- Do the balance of benefits and risks and facilitation of implementation warrant an update to COVID-19 vaccine policy?

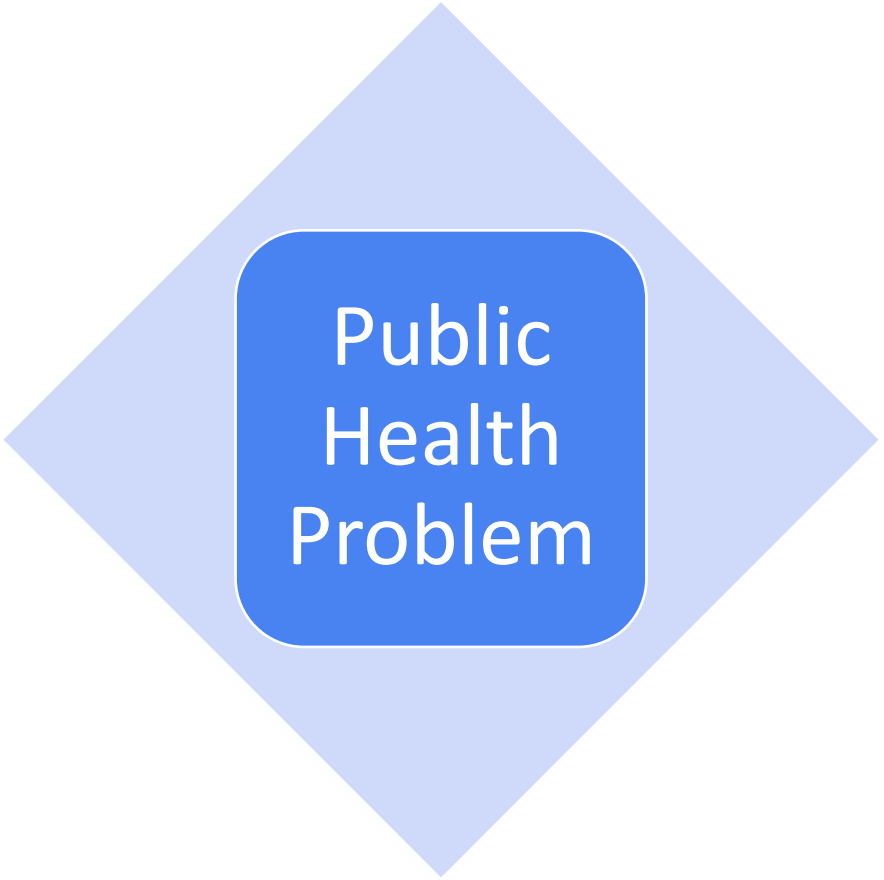
All other persons ≥18 years of age **may** receive a COVID-19 booster dose ≥6 months after completion of the mRNA primary series under the current Emergency Use Authorization

Persons who may receive a COVID-19 booster dose, based on individual benefits and risks

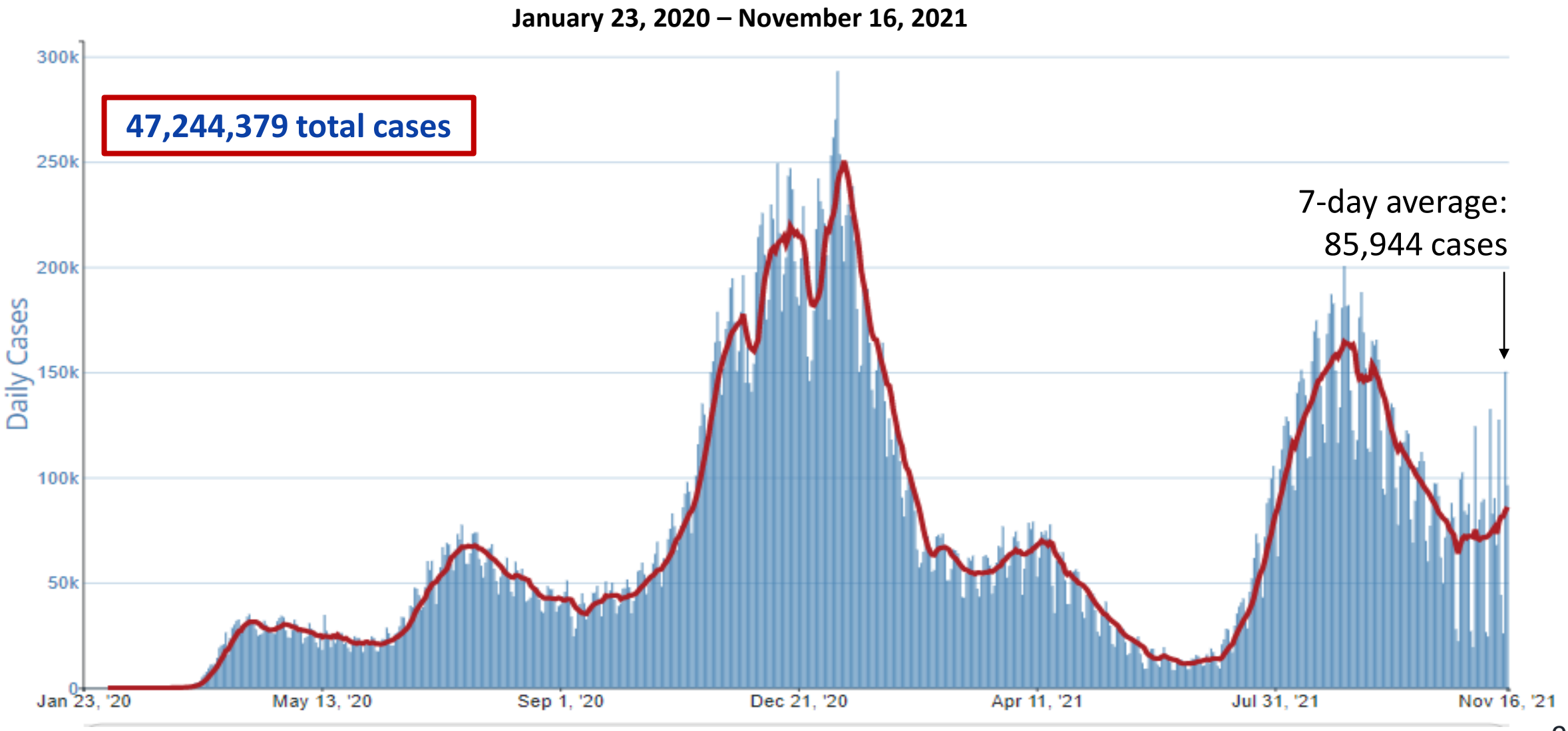
- Aged 18-49 years with certain underlying medical conditions*
- Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting
- All other persons aged ≥18 years

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines



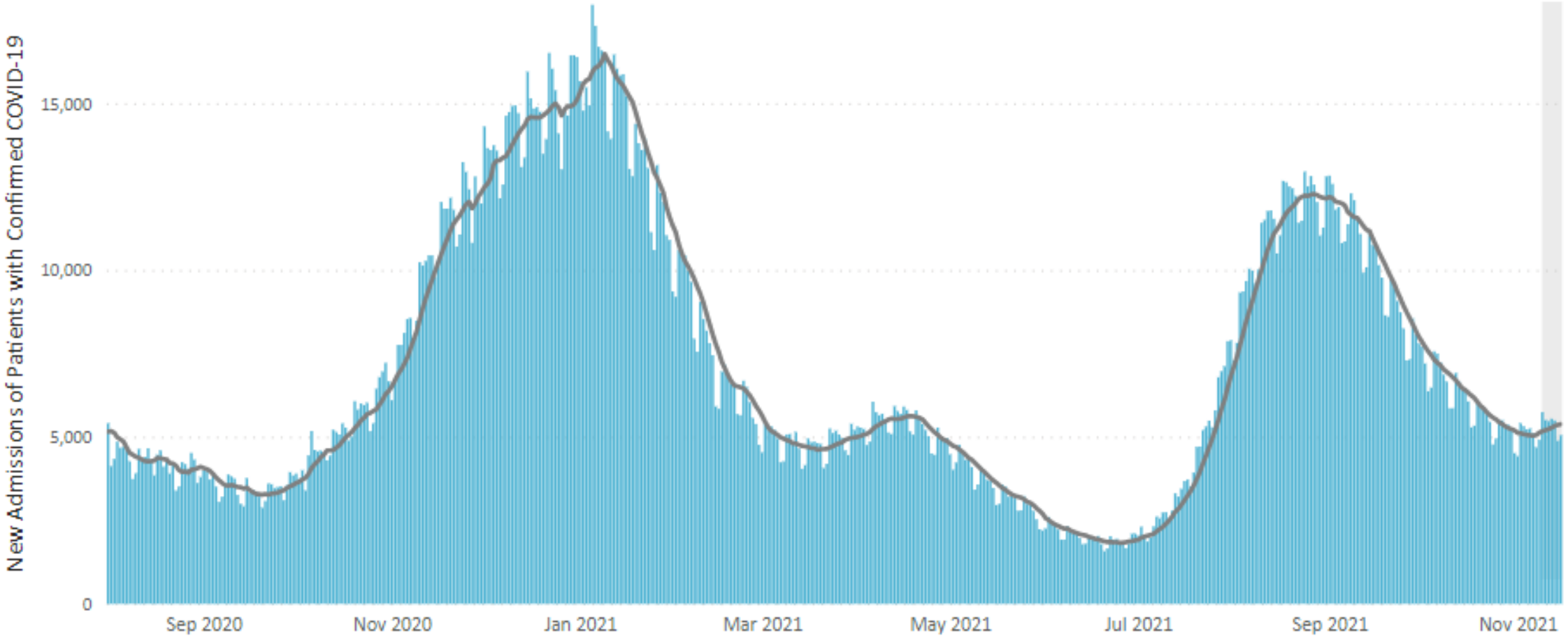
Trends in COVID-19 cases in the United States



CDC. https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. Accessed November 18, 2021

Trends in COVID-19 hospitalizations in the United States

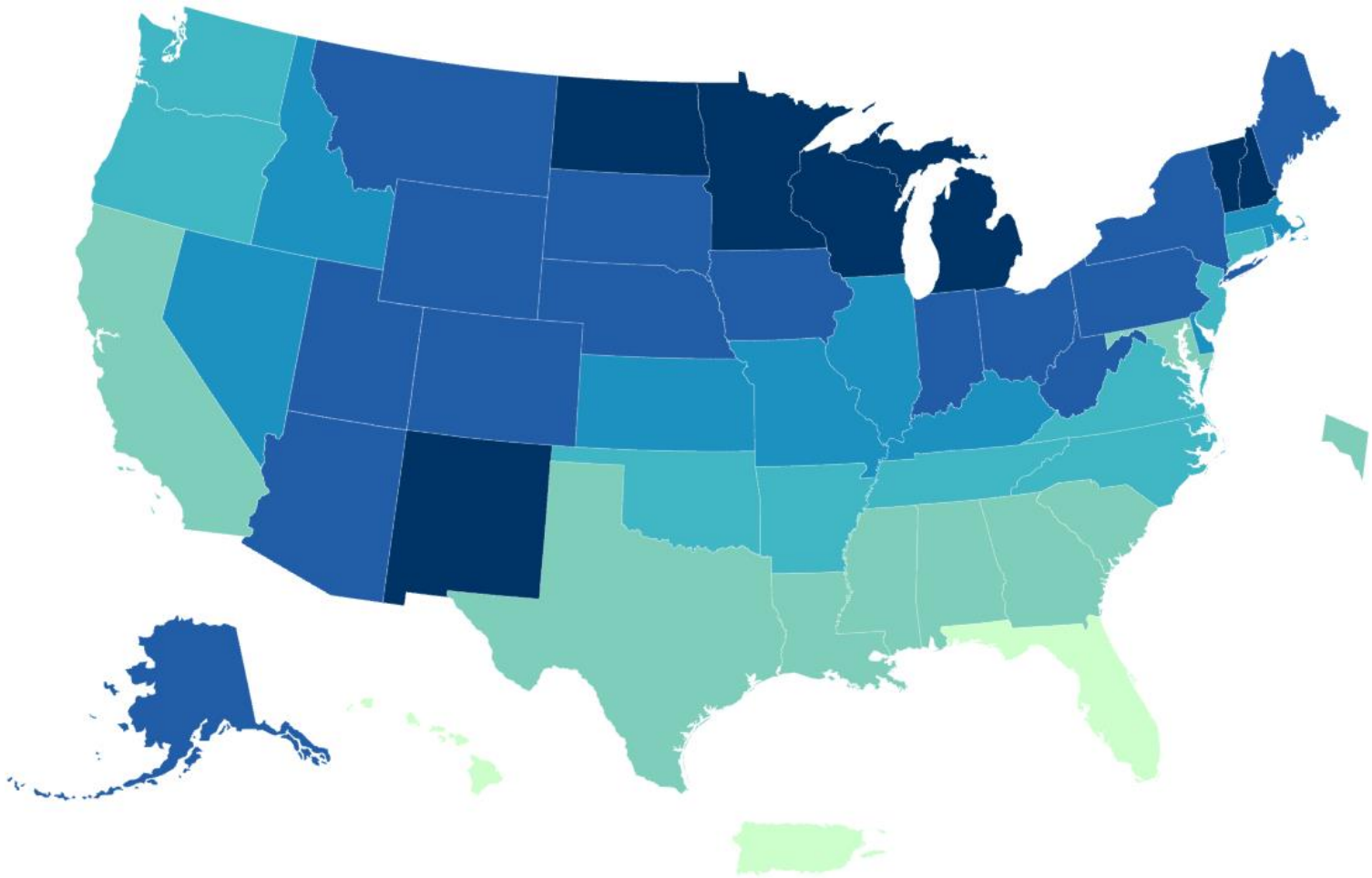
August 1, 2020 – November 15, 2021



CDC: https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions Accessed November 17, 2021

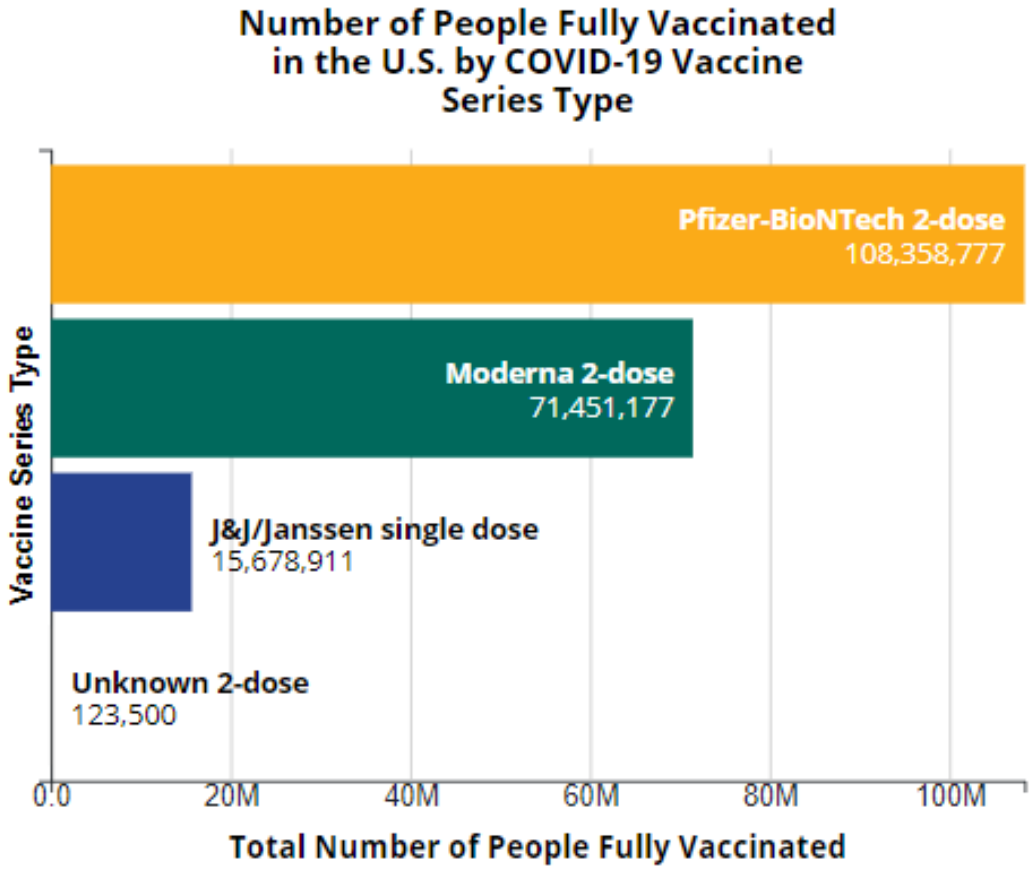
US COVID-19 7-day case rate per 100,000

By state/territory



CDC: https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days Accessed November 18, 2021

Number of people fully vaccinated in the U.S. by COVID-19 vaccine series type

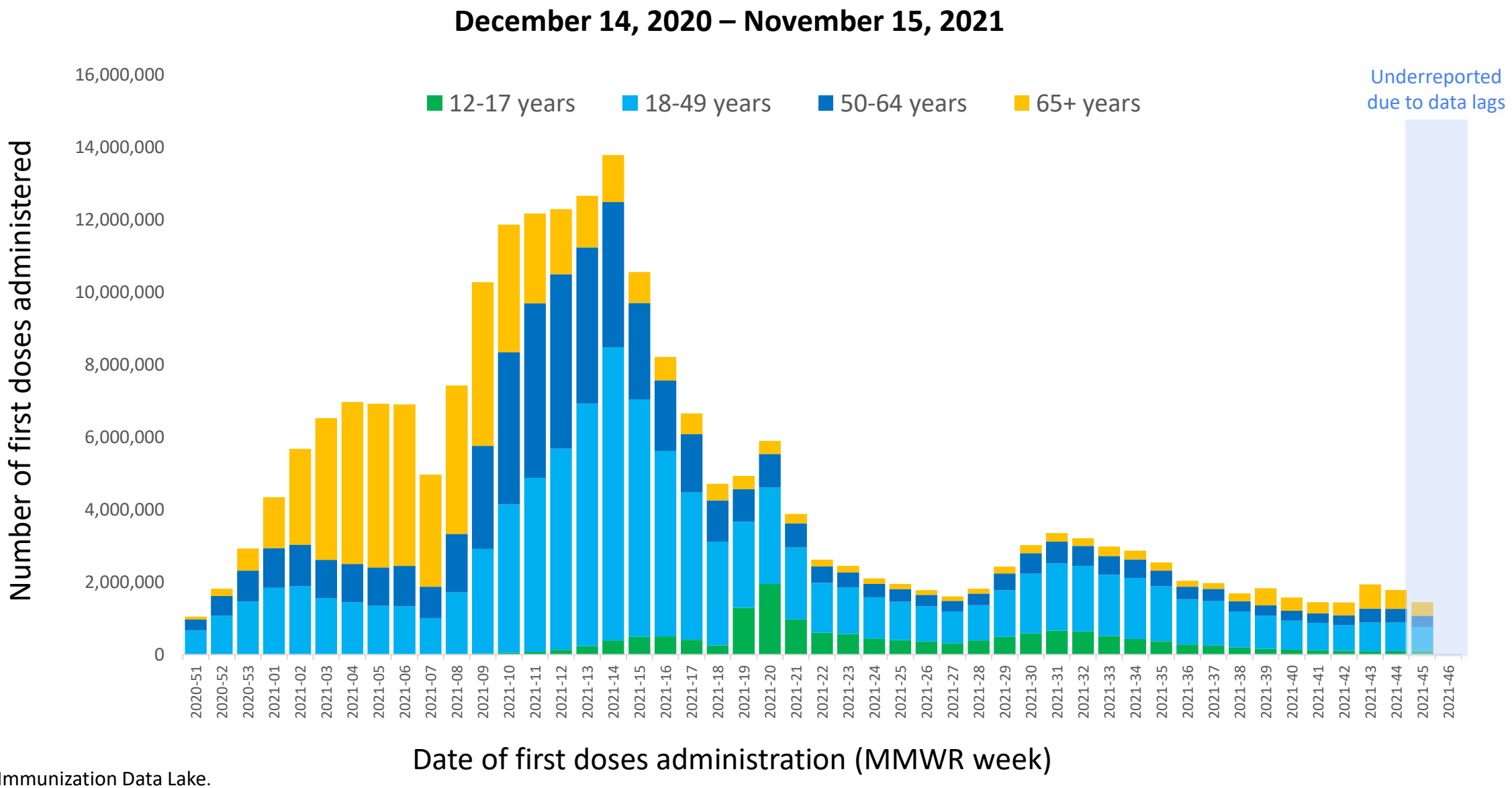


Over **195** million people fully vaccinated in the US

69% of the population ≥12 years of age

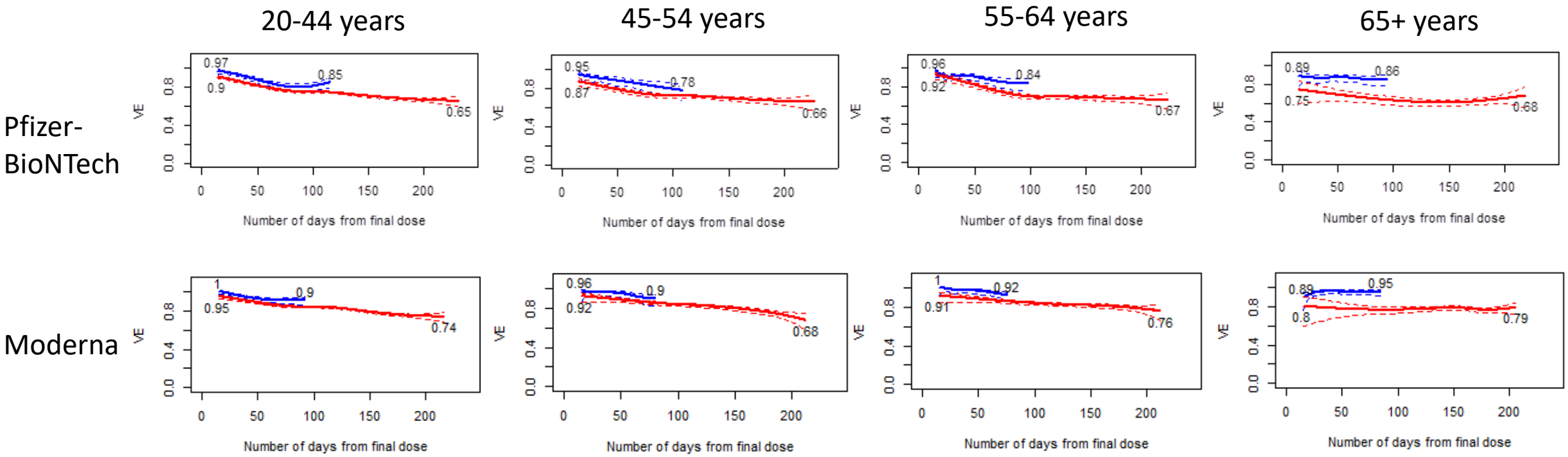
CDC. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-12yr. Accessed November 18, 2021

COVID-19 vaccine first doses administered, by age group



Source: Immunization Data Lake.

VE against symptomatic infection by age group and time since vaccination in pre-Delta and Delta periods



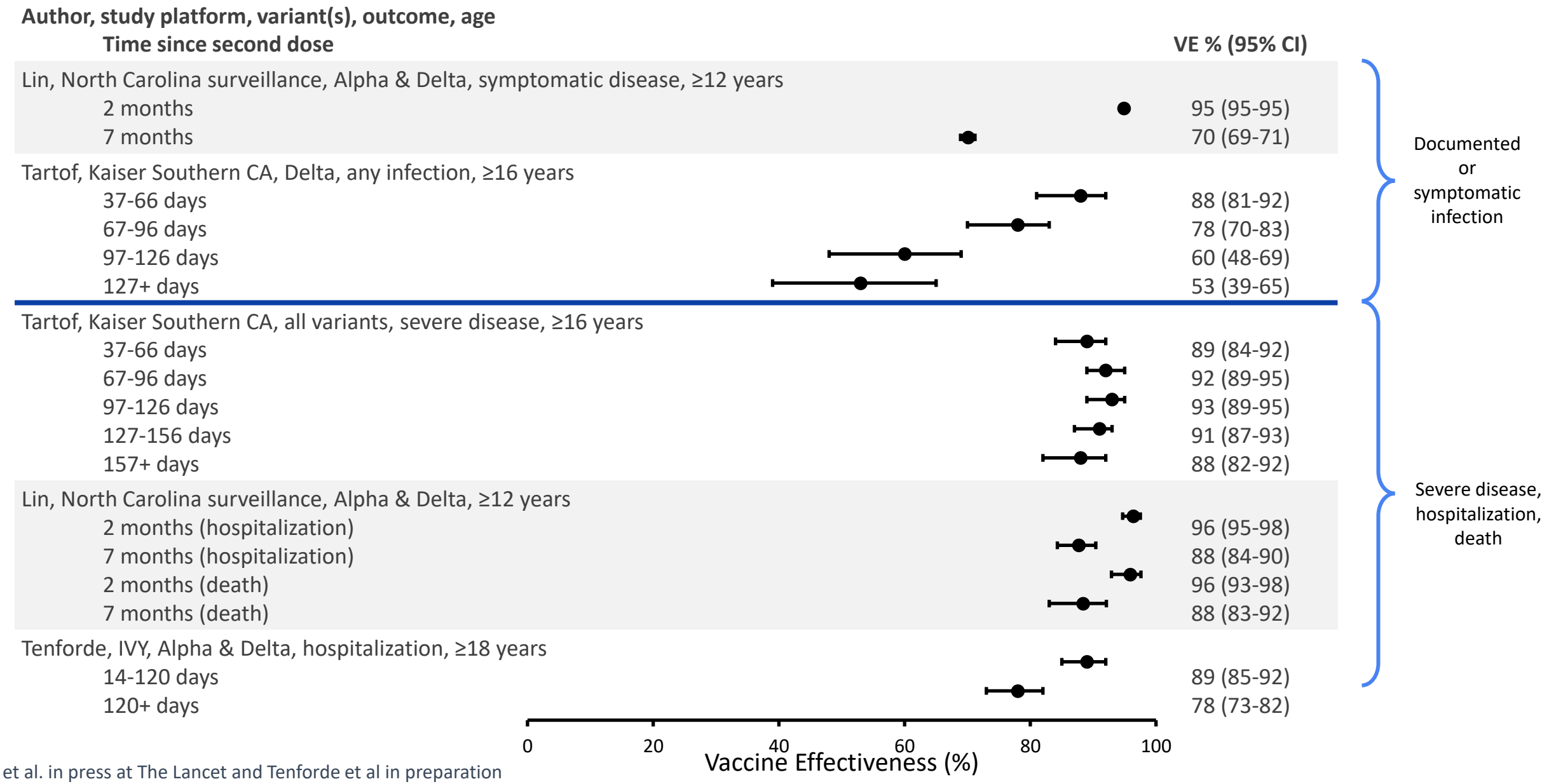
Pre-Delta (March 13–May 29) with 95% CIs in dotted lines

Delta (July 18–August 31) with 95% CIs in dotted lines

- VE is lower during Delta
- VE wanes during both periods
- Curves similar across age groups
- For ≥65, VE lower than for other age groups soon after vaccination, no clear trend over time since vaccination

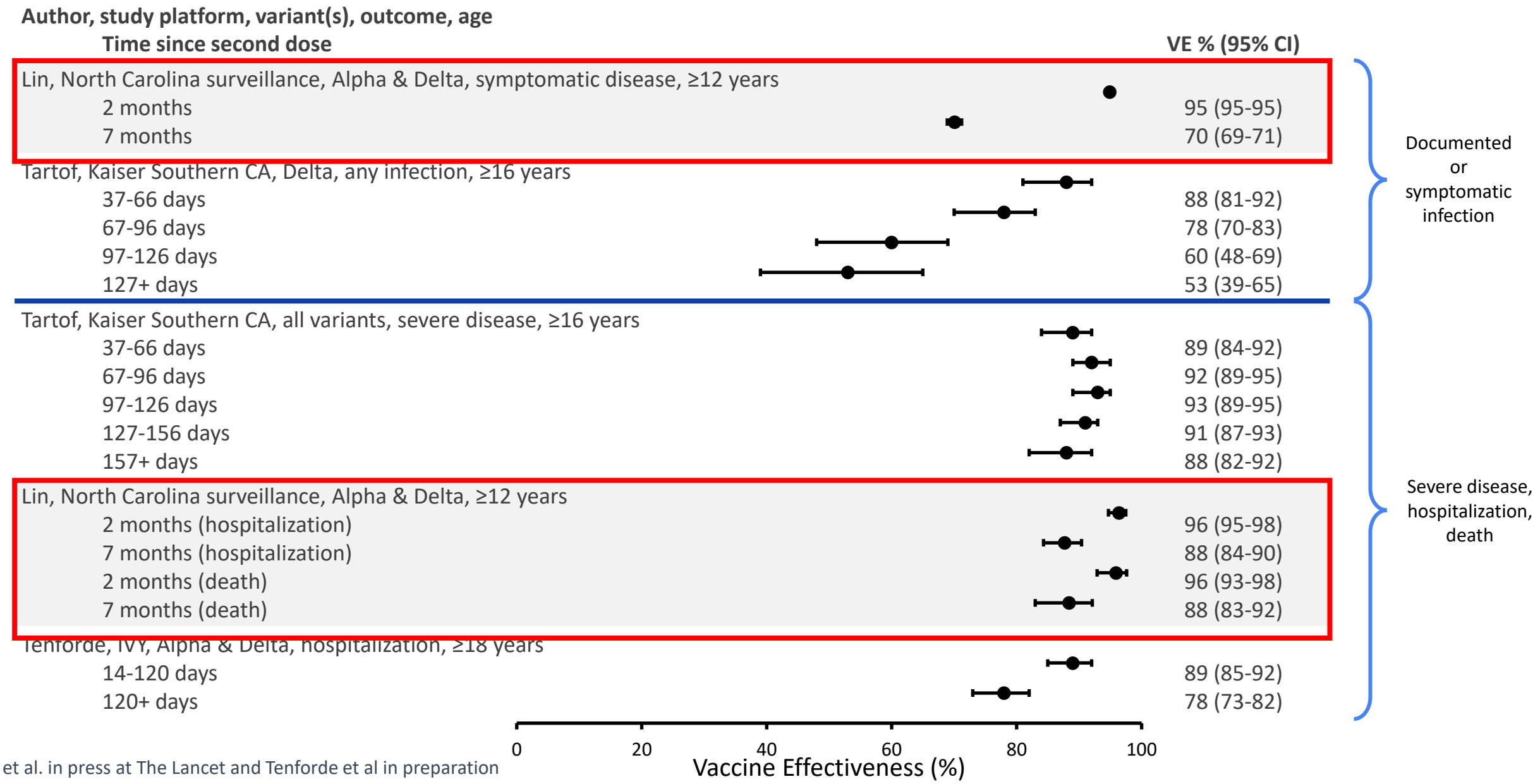
The presented (fitted) curves are truncated on the day with ≤10 cases observed beyond it to avoid presenting wide confidence bounds.

Vaccine effectiveness for Pfizer-BioNTech vaccine by time since second dose, outcome, and age



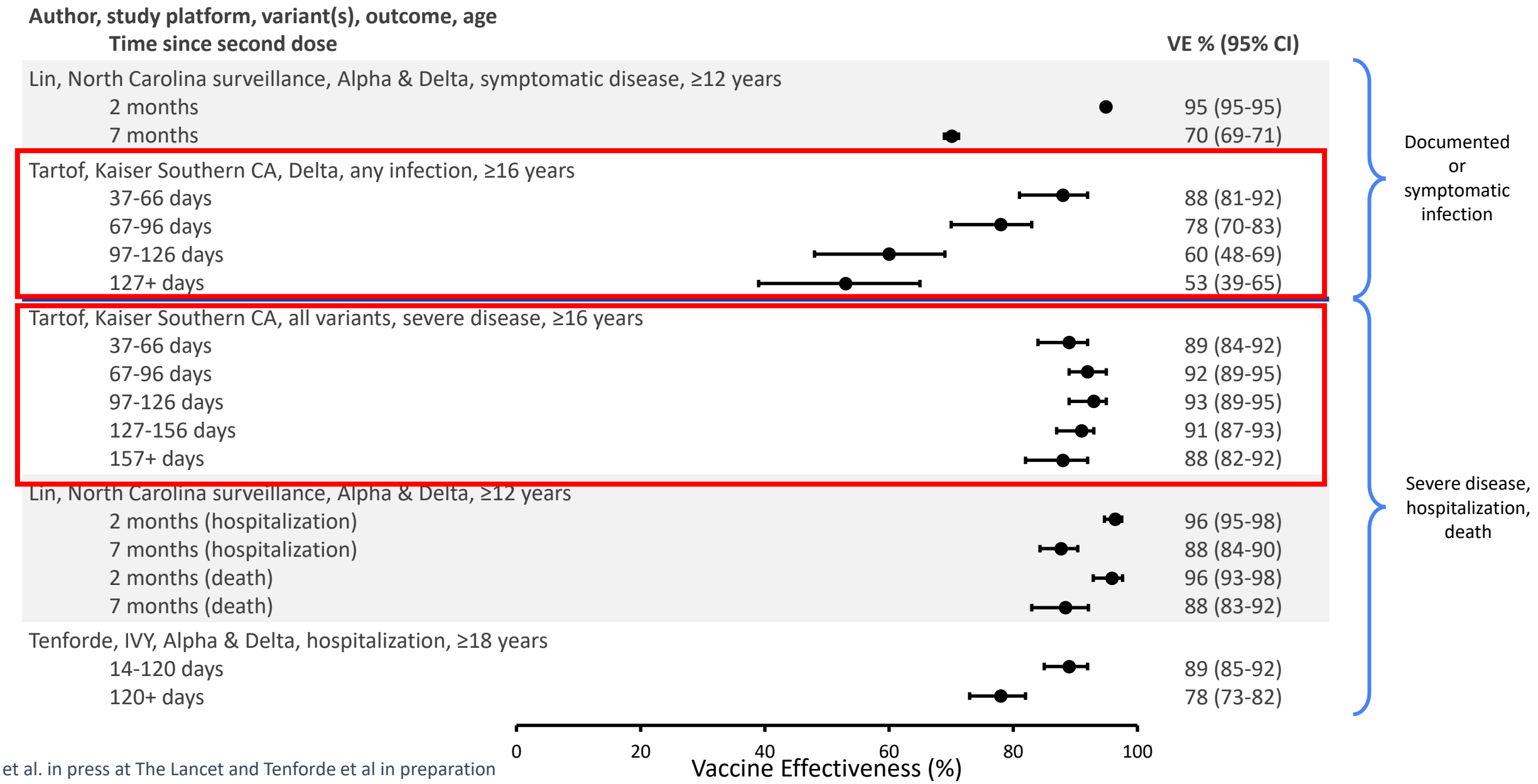
Feikin et al. in press at The Lancet and Tenforde et al in preparation

Vaccine effectiveness for Pfizer-BioNTech vaccine by time since second dose, outcome, and age



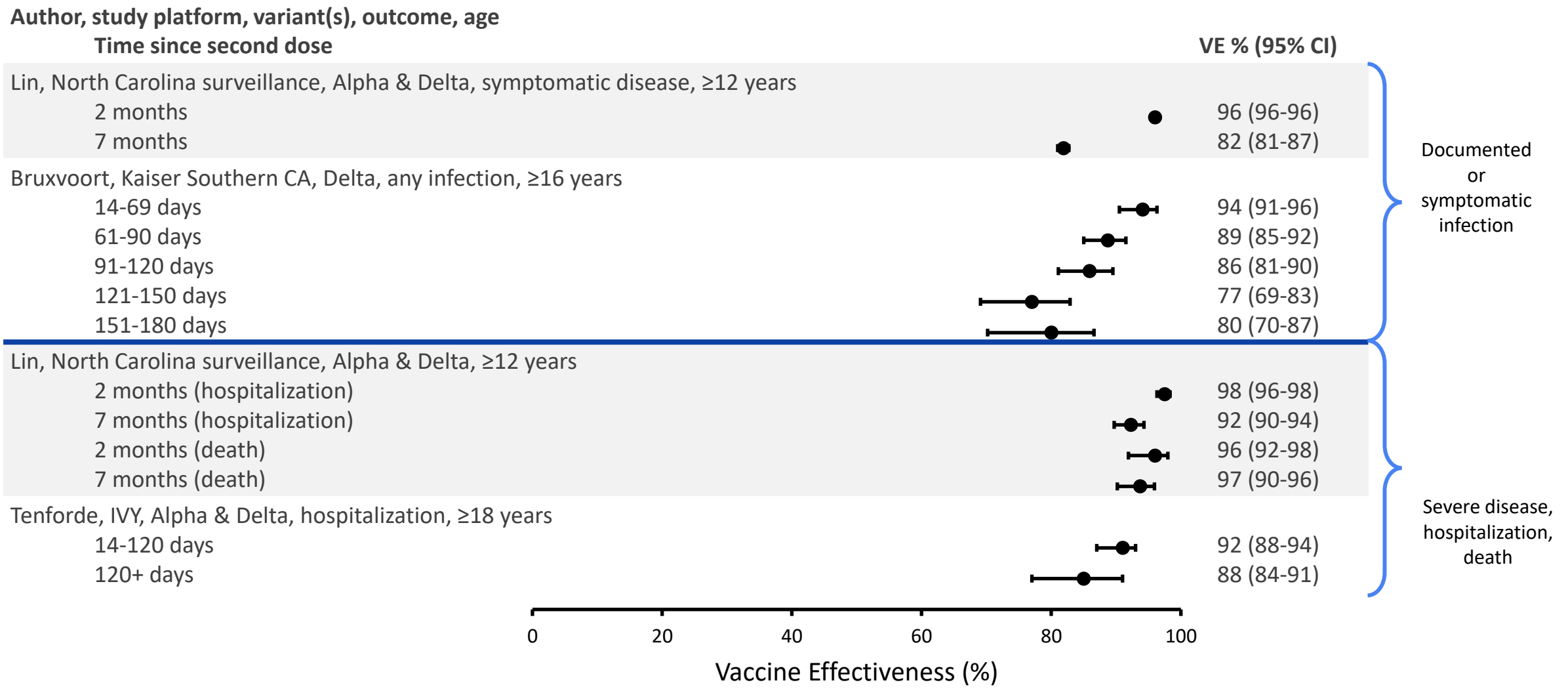
Feikin et al. in press at The Lancet and Tenforde et al in preparation

Vaccine effectiveness for Pfizer-BioNTech vaccine by time since second dose, outcome, and age



Feikin et al. in press at The Lancet and Tenforde et al in preparation

Vaccine effectiveness for Moderna vaccine by time since second dose, outcome, and age



Feikin et al. in press at The Lancet and Tenforde et al in preparation

Summary

- Over 195 million people are fully vaccinated in the United States
- COVID-19 cases are increasing in some jurisdictions recently
- VE after primary series waning for infection, but protection remains high for severe disease and hospitalization
  - Waning appears to be less pronounced for Moderna COVID-19 vaccine, compared to Pfizer-BioNTech COVID-19 vaccine recipients

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

PICO Question

	Pfizer-BioNTech	Moderna
Population	Persons aged ≥18 years who completed a COVID-19 vaccine primary series ≥6 months ago	
Intervention	Pfizer-BioNTech COVID-19 Vaccine booster dose (BNT162b2, 30 µg, IM)	Moderna COVID-19 Vaccine booster dose (mRNA-1273, 50 µg, IM)
Comparison	No booster dose	
Outcomes	Symptomatic laboratory-confirmed COVID-19* Hospitalization due to COVID-19* Death due to COVID-19 Transmission of SARS-CoV-2 infection Serious adverse events* Reactogenicity	

* Critical outcomes

Updated Pfizer-BioNTech booster data

- Phase 3 booster dose randomized control trial (RCT)
- ~10,000 participants from phase 2/3 efficacy trial
  - All participants received 2-dose primary series of Pfizer-BioNTech COVID-19 vaccine
- Pfizer-BioNTech booster dose and placebo doses randomized 1:1
  - Randomization was stratified by age
    - 60% 16-55 years
    - 40% >55 years
  - Booster doses given 10-12 months after second dose
- Median follow-up of 2.5 months post booster dose

Clinical trial data requested by CDC.

Outcome 1: Symptomatic laboratory-confirmed SARS-CoV-2 infection

Population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Relative vaccine efficacy (95% CI)
Primary Outcome			
No evidence of prior infection, ≥7 days post booster	6/4659	123/4614	95.2% (89.3%, 97.9%)
Secondary Outcomes			
± evidence of prior infection, ≥7 days post booster	7/4994	124/4963	94.5% (88.3%, 97.4%)
All available efficacy (± evidence of prior infection, post booster)	15/5003	141/4943	89.8% (82.6%, 94.0%)
0-7 days post booster	8/5003	15/4943	47.4% (-24.0%, 77.7%)
≥7 days to <2 months post booster	6/4995	112/4928	94.9% (88.5%, 97.8%)
≥2 months to <4 months post booster	1/4891	14/4616	93.3% (48.9%, 99.1%)

Clinical trial data requested by CDC.

Outcome 1: Symptomatic laboratory-confirmed SARS-CoV-2 infection

Population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Relative vaccine efficacy (95% CI)
Primary Outcome			
No evidence of prior infection, ≥7 days post booster	6/4659	123/4614	95.2% (89.3%, 97.9%)
Secondary Outcomes			
± evidence of prior infection, ≥7 days post booster	7/4994	124/4963	94.5% (88.3%, 97.4%)
All available efficacy (± evidence of prior infection, post booster)	15/5003	141/4943	89.8% (82.6%, 94.0%)
0-7 days post booster	8/5003	15/4943	47.4% (-24.0%, 77.7%)
≥7 days to <2 months post booster	6/4995	112/4928	94.9% (88.5%, 97.8%)
≥2 months to <4 months post booster	1/4891	14/4616	93.3% (48.9%, 99.1%)

Clinical trial data requested by CDC.

Evaluation of other beneficial outcomes

- Hospitalization due to COVID-19
  - No hospitalizations due to COVID-19 occurred in the booster (3-dose) or placebo (2-dose) groups
- Death due to COVID-19
  - No deaths due to COVID-19 occurred in the booster (3-dose) or placebo (2-dose) groups
- Transmission of SARS-CoV-2 infection
  - No data to assess this outcome

Clinical trial data requested by CDC.

Outcome 6: Serious Adverse Events

Study/population[a]	Events/Vaccine (n/N)	% SAE Vaccine	Events/Placebo (n/N)	% SAE Placebo	Associated with vaccination[b]
Pfizer/BioNTech, unpublished	16/5055	0.3	24/5020[c]	0.5	3

a. Included all randomized participants who received a booster dose
b. Three serious adverse events among booster recipients were deemed by blinded investigators to be related to vaccination. These included: moderate persistent tachycardia, moderate transient elevated hepatic enzymes, and mild elevated hepatic enzymes.
c. There was one death among placebo recipients and none among booster dose recipients

Adverse events of clinical interest

- No cases of anaphylaxis, hypersensitivity, or myocarditis/pericarditis reported
  - Given the rarity of these adverse events, we would not expect to capture them in a RCT of this size
- Lymphadenopathy was more common after the 3rd dose (**2.7**%) than after the primary series (**0.4**%)
  - Typically mild to moderate and located in the axilla or cervical nodes
  - Most occurred 1-3 days post booster and resolved within 1-3 days of onset
  - Frequency higher in younger participants and female participants

Clinical trial data requested by CDC.

Outcome 7: Reactogenicity

- No updated data from phase 3 booster trial

Pfizer-BioNTech booster ≥6 months after primary series

Changes to GRADE from previous booster discussion

Outcome	Importance	Previous evidence certainty	Current evidence certainty
Benefits			
Symptomatic laboratory-confirmed COVID-19	Critical	Very low	**High**
Hospitalization due to COVID-19	Critical	Very low	**Very low**
Death due to COVID-19	Important	No data	**No data**
Transmission of SARS-CoV-2 infection	Important	No data	**No data**
Harms			
Serious adverse events	Critical	Very low	**Low**
Reactogenicity	Important	Very low	**Very Low**

Myocarditis in Israel

Reported after Pfizer-BioNTech COVID-19 vaccine, December 2020-October 10, 2021

	Age (years)	Post-dose 1 Rate per 100,000	Post-dose 2 Rate per 100,000	Post-dose 3 Rate per 100,000	Number of 3rd dose delivered
Females	12-15	0	0.6	0	279
	16-19	0	0.9	0	97,807
	20-24	0.4	2.5	0	141,910
	25-29	0	0.4	0	130,283
	≥30	0.1	0.3	0	1,542,142
Males	12-15	0.5	6.6	0	292
	16-19	1.2	16.1	5.2	96,238
	20-24	2.2	10.3	3.6	139,015
	25-29	1.2	8.4	0.7	133,650
	≥30	0.5	1.7	0.4	1,448,745

Rates of myocarditis after a third dose appear to fall **between** rates seen after **dose 1** and **dose 2**

As reported by Israel at FDA's VRBPAC meeting. Slides here: https://www.fda.gov/media/153086/download .

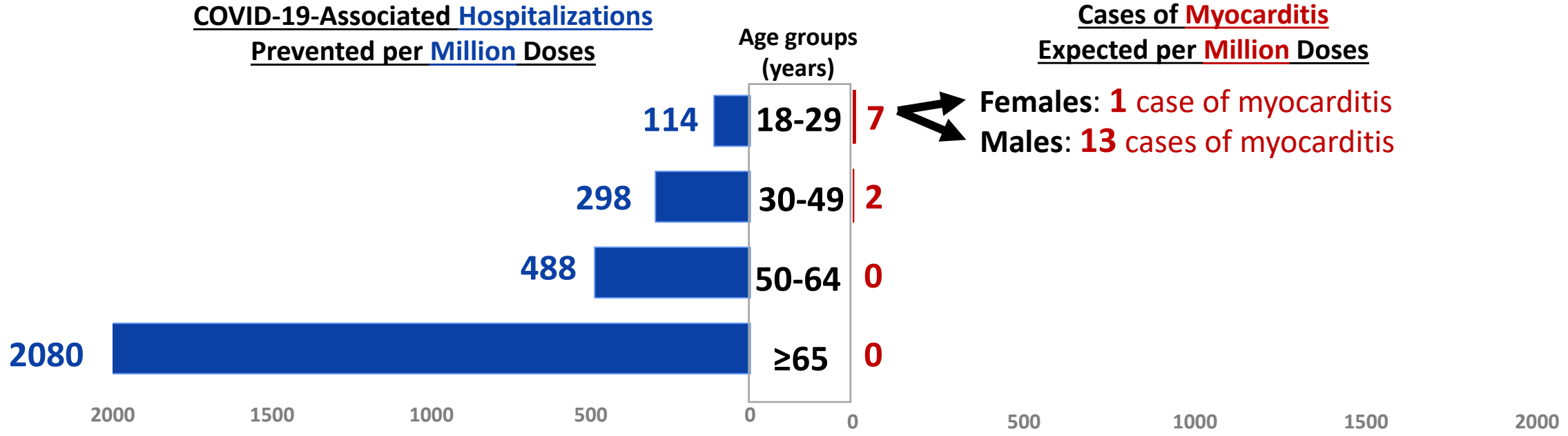
Benefits and risks after Pfizer-BioNTech COVID-19 booster dose

For every million doses of vaccine given

Scenario:

- VE for hospitalization averaged from four platforms[1]
- Boost to 95% VE for hospitalization
- **Myocarditis risk equivalent to risk after 1st and 2nd dose averaged**

Age Group	VE for hospitalization
18 – 29 years	90.7%
30 – 49 years	90.2%
50 – 64 years	91.1%
≥65 years	85.1%



1. Scobie et al., COVID-NET, VISION, IVY Network

COVID-NET hospitalization rates from the week of August 21, 2021; Myocarditis rates from VAERS data through August 18, 2021

Benefits and risks after Pfizer-BioNTech COVID-19 booster dose

- Phase 3 RCT booster efficacy data demonstrates booster dose provides additional protection and is safe
  - No hospitalized cases of COVID-19 after 2-dose primary series

- Based on data from Israel, myocarditis risk after booster dose of Pfizer-BioNTech COVID-19 vaccine appears to fall between rates seen after dose 1 and dose 2

Moderna booster data

No booster vaccine efficacy/effectiveness studies identified

Moderna booster study previously presented*

- Part A: Phase 2 randomized, observer-blind, placebo-controlled dose confirmation study among participants aged ≥18 years
- Part B: study amended for open label phase based on participant selection
  - Placebo recipients → 100 µg primary series
  - 50 µg primary series → 50 µg booster (≥6 months after dose 2)
  - 100 µg primary series → 50 µg booster (≥6 months after dose 2)
- Immunobridging to patients in Phase 3 efficacy study
  - Prespecified non-inferiority analysis
  - 28 days after booster versus 28 days after dose 2 of primary series

*Unpublished data obtained from the study sponsor: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/02-COVID-Miller-508.pdf

Moderna booster data

- Symptomatic laboratory-confirmed COVID-19
  - Geometric mean titers of booster recipients (N=149) compared to primary series recipients (N=1,053)
  - The geometric mean ratio of 1.76 (95%CI: 1.50–2.06) met non-inferiority criteria
- Serious Adverse Events
  - No SAEs occurred among the 171 participants receiving a 50 ug booster in the open label booster study within 28 days of the booster dose
- Reactogenicity
  - Severe reactogenicity occurred among 10.8% of participants receiving a booster in the open label booster study

Moderna booster ≥6 months after primary series

Summary of GRADE – No update to previous discussion

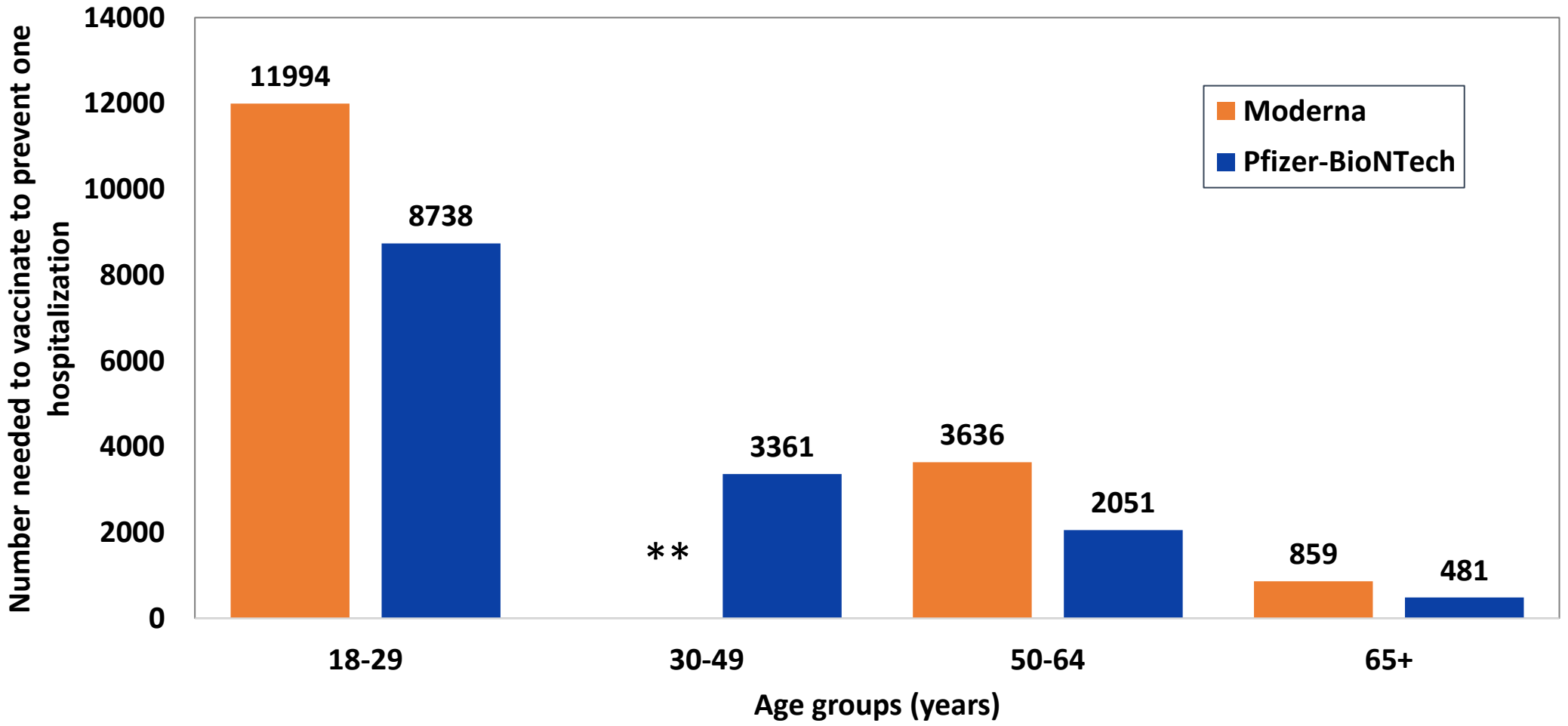
Outcome	Importance	Evidence certainty
Benefits		
Symptomatic laboratory-confirmed COVID-19	Critical	**Very low**
Hospitalization due to COVID-19	Critical	**No data**
Death due to COVID-19	Important	**No data**
Transmission of SARS-CoV-2 infection	Important	**No data**
Harms		
Serious adverse events	Critical	**Very low**
Reactogenicity	Important	**Very low**

Benefits and risks after Moderna COVID-19 booster dose

- No phase 3 RCT booster efficacy data available for Moderna
  - Immunogenicity study demonstrates the ability to boost antibody levels
- Effectiveness after a primary series appears to have waned less in Moderna than in Pfizer

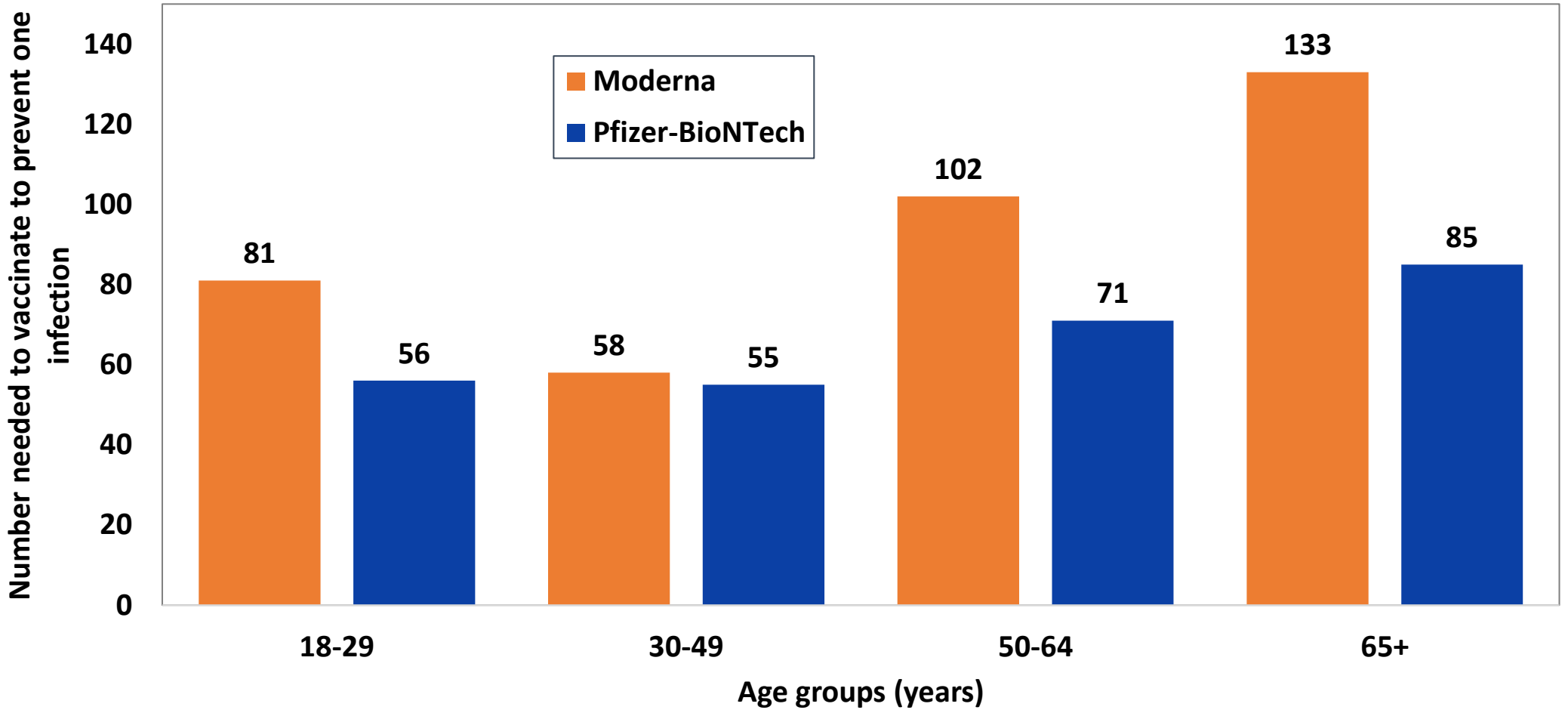
- Myocarditis risk after booster dose of Moderna is unknown
  - Accumulating evidence from multiple sources suggests a higher risk for myocarditis following Moderna compared to Pfizer-BioNTech primary series vaccination
  - Moderna booster dose is a lower dose (50µg) than the primary series dose (100µg)

Number needed to vaccinate with booster dose to prevent one hospitalization over 6 months



** Not estimable due to pre-booster efficacy estimated at >95%

Number needed to vaccinate with booster dose to prevent one infection over 6 months



Summary of safety surveillance findings

- V-safe
  - For Pfizer-BioNTech and Moderna, local and systemic reactions were reported less frequently following a booster dose than dose 2 of the primary series
  - Moderna booster appears to be more reactogenic than Pfizer-BioNTech booster, regardless of the primary series manufacturer
- VAERS
  - Most reports (≥93%) were non-serious (similar to primary series)
  - Most frequently reported non-serious AEs were known and well characterized AEs associated with COVID-19 vaccination
  - 54 preliminary reports of myocarditis
    - 12 verified reports that met CDC case definition

Impact of a booster dose on transmission

- After a primary mRNA COVID-19 vaccine series, protection against **asymptomatic infection** (and presumably transmission) was found for a time period[1,2]
  - Largest impact seen in the first 2 months post-vaccination[2]
  - Likely an impact of very high antibody titers
- Limited data on impact of booster dose on asymptomatic infection/transmission
  - One study from Israel found **lower viral loads** in patients with breakthrough infections after a booster dose, similar to viral loads seen within 2 months after primary series[2]
  - Early VE against SARS-CoV-2 infection after a booster dose demonstrates increase in VE (including asymptomatic infection)[3,4]
- While protection against asymptomatic infection may not be permanent, even temporary protection may favor into benefit/risk balance approaching winter and holidays with increased travel and indoor gatherings

[1]CDC Science Brief https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html [2]Levine-Tiefenbrun et al. Nature Medicine 2021 https://www.nature.com/articles/s41591-021-01575-4
[3]Saciuk et al. Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab556/6415586
[4]Andrews et al. Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against covid-19 related symptoms in England: test negative case-control study | medRxiv

Summary

Balance of benefits and harms for booster doses

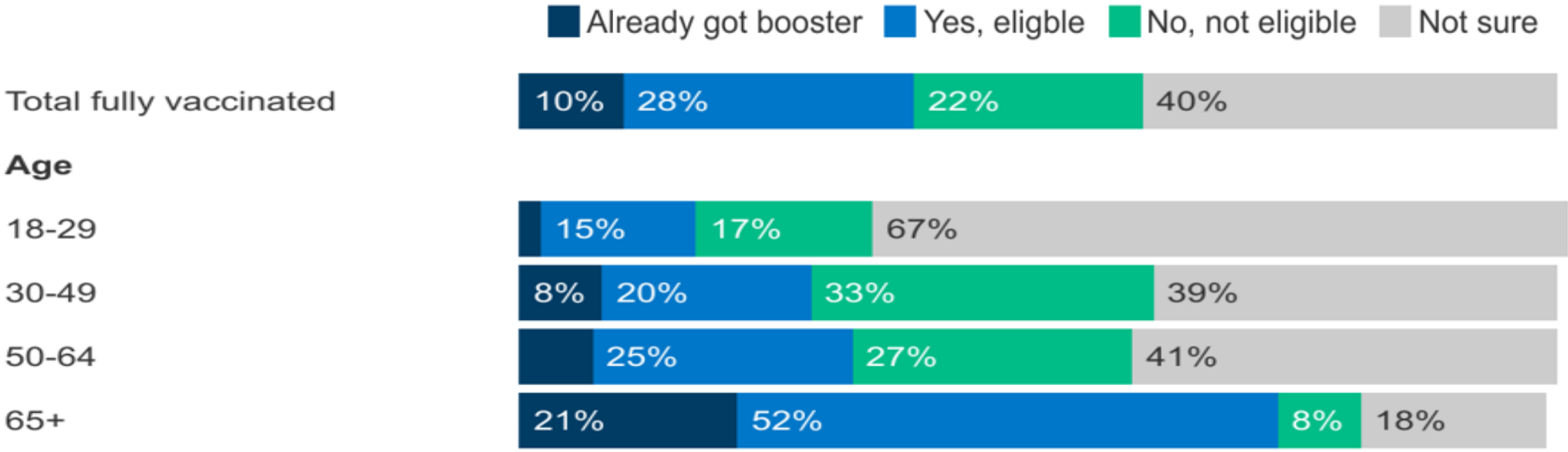
- Booster dose of Pfizer-BioNTech COVID-19 vaccine is **effective** in preventing laboratory confirmed symptomatic SARS-CoV-2
- Data from Moderna trial does not provide efficacy data, but demonstrates the ability to boost immune response
- Individual benefit/risk balance for booster doses of an mRNA vaccine **varies by age**
  - Older adults have the clearest benefit/risk balance
  - Among other ages, variation within balance of benefits and risks
  - Myocarditis data after booster doses reassuring to date
- Unable to account for other benefits
  - Possible impact on rates of community transmission

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Survey of fully vaccinated adults (vaccine booster eligibility)

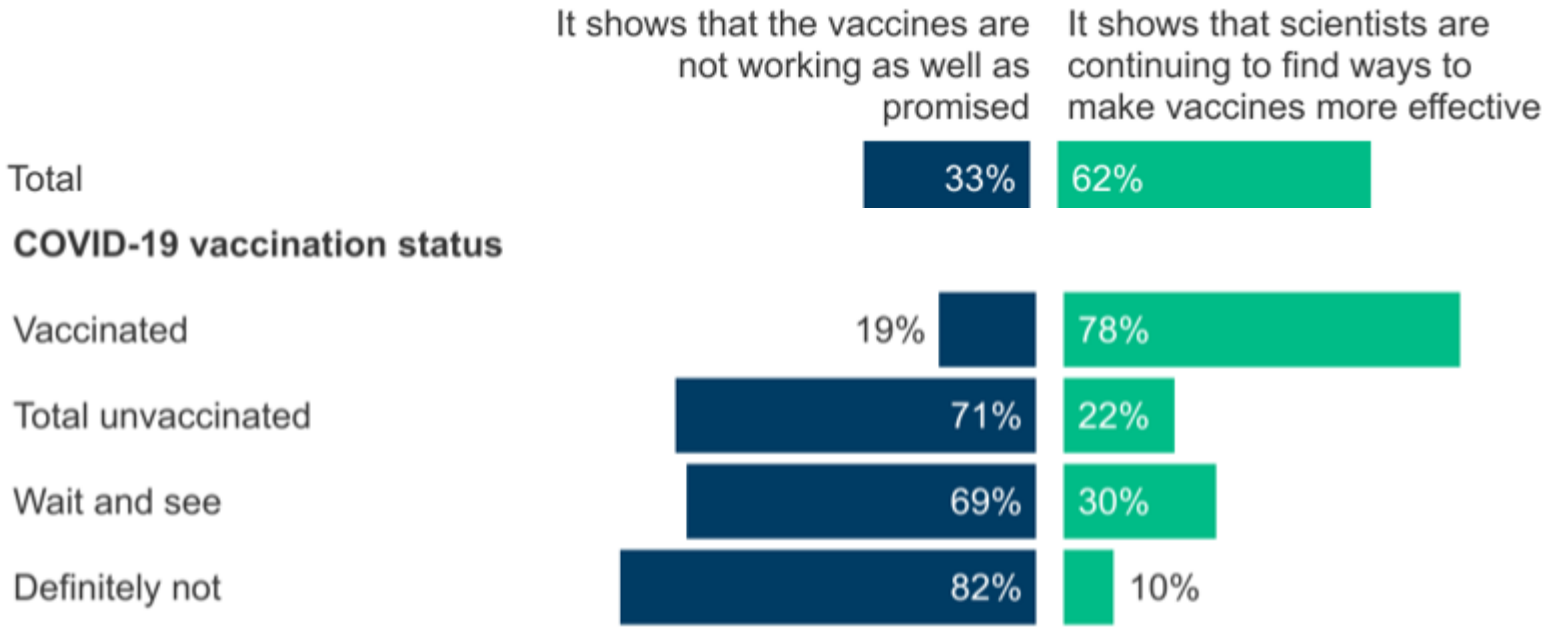
- Survey respondents were asked:
  - *"Have you personally received a booster or additional dose of the COVID-19 vaccine after you were already fully vaccinated?"*
  - **4 in 10** fully vaccinated adults are **unsure** whether they are eligible for a booster dose



KFF COVID-19 Vaccine Monitor (October 14-24, 2021) KFF COVID-19 Vaccine Monitor: October 2021 | KFF

Vaccine booster confidence

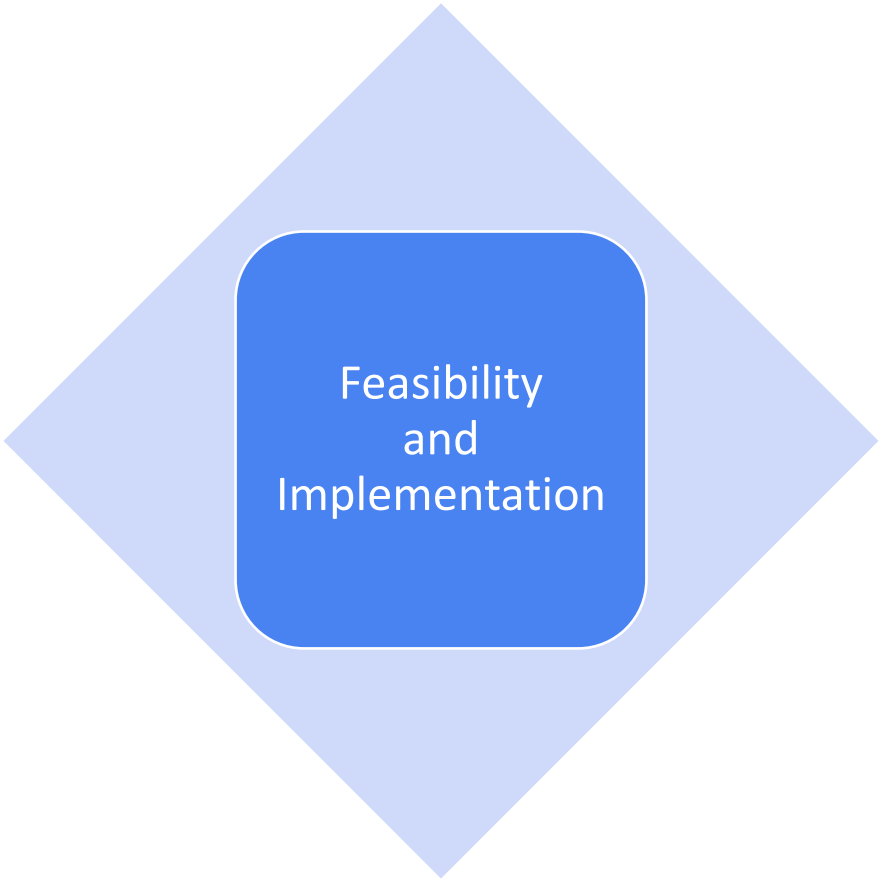
- Survey respondents were asked:
  - *"Which comes closer to your view about the news that some people might need vaccine boosters?"*
  - **More than 6 in 10** adults overall say the news that some people might need boosters **"shows that scientists are continuing to find ways to make vaccines more effective."**



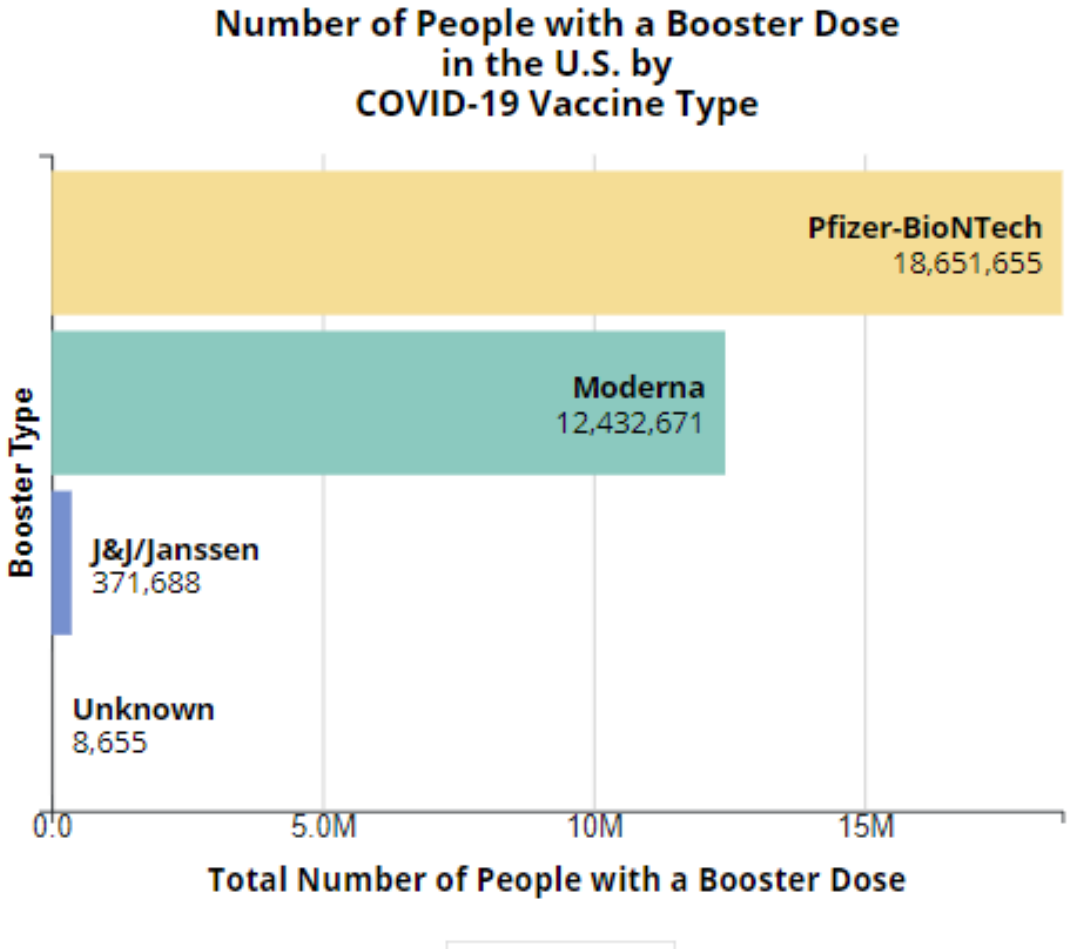
KFF COVID-19 Vaccine Monitor (September 13-22, 2021) KFF COVID-19 Vaccine Monitor: September 2021 | KFF

Evidence to Recommendations Framework

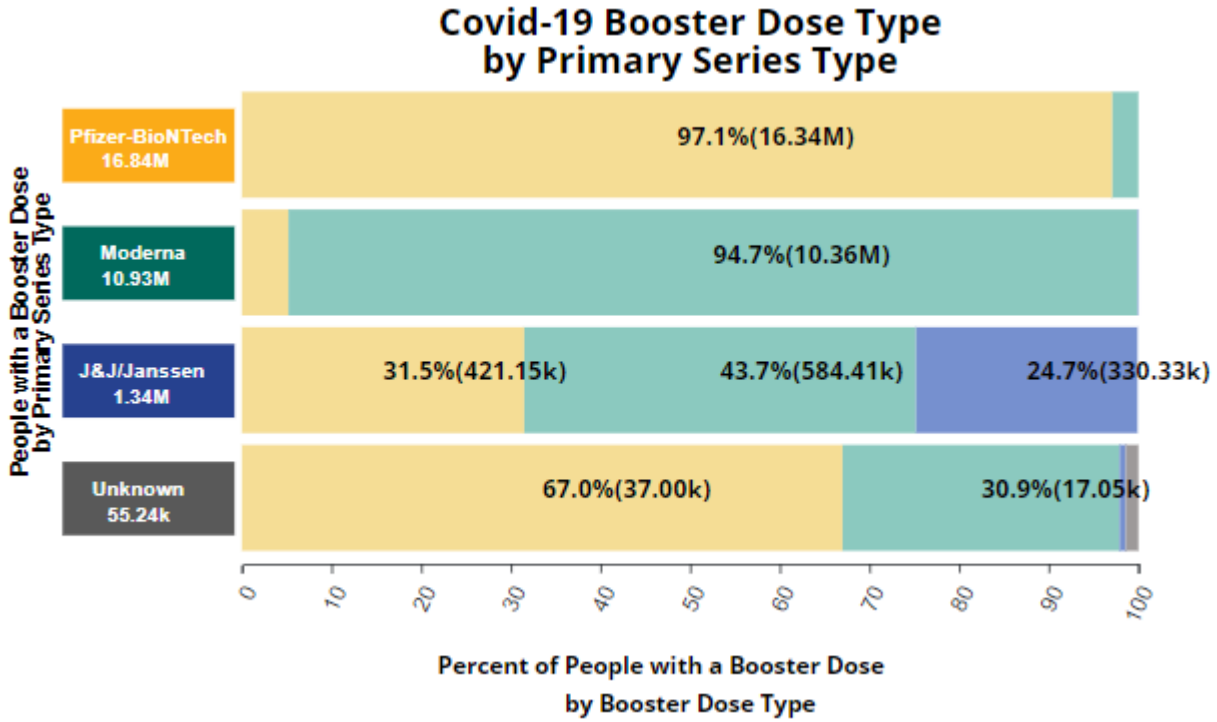
Booster doses of COVID-19 vaccines



Number of people with a booster dose in the U.S. by COVID-19 vaccine series type



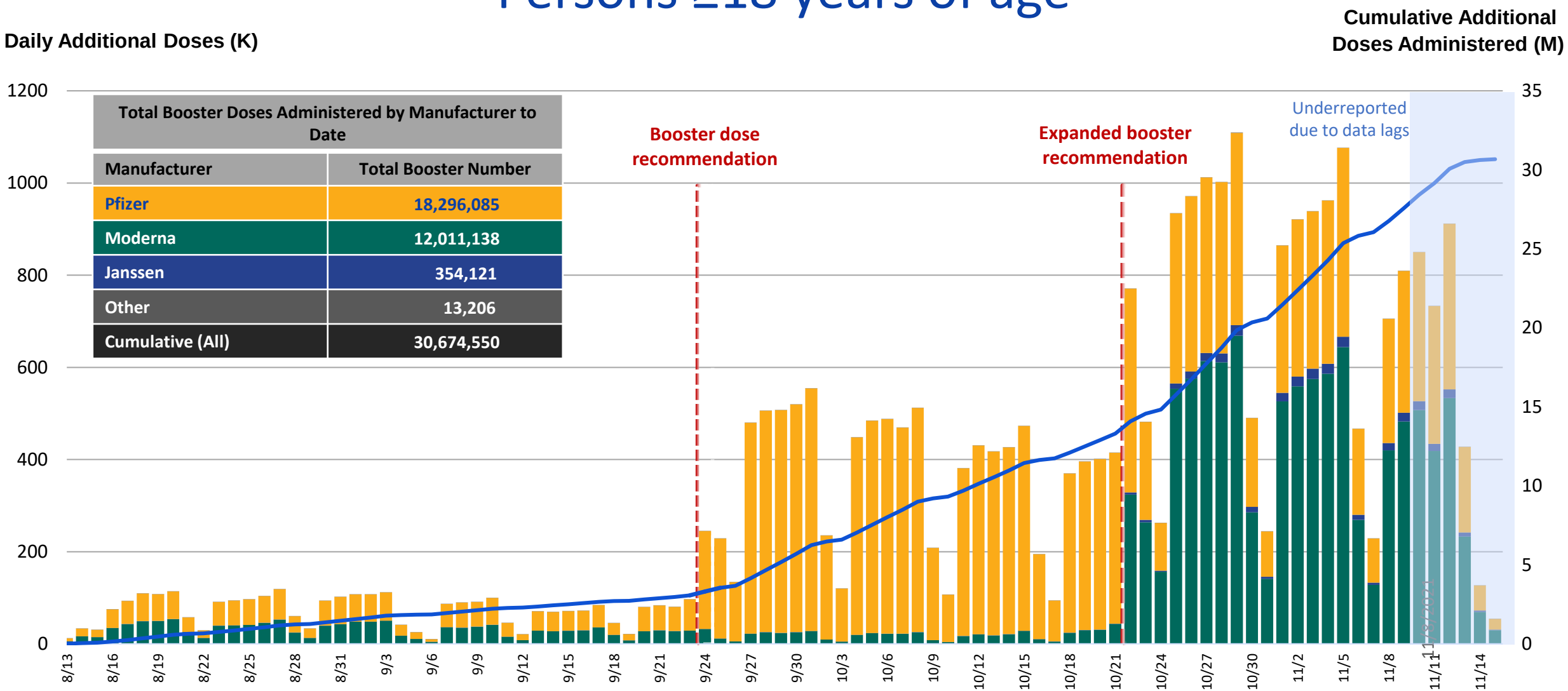
Over **31** million people have received a booster dose in the US



CDC. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-12yr. Accessed November 18, 2021

Daily number of booster doses administered, by manufacturer

Persons ≥18 years of age



Total Booster Doses Administered by Manufacturer to Date	
Manufacturer	Total Booster Number
Pfizer	18,296,085
Moderna	12,011,138
Janssen	354,121
Other	13,206
Cumulative (All)	30,674,550

Note: Number of people who received a booster dose includes anyone who is fully vaccinated and has received another dose of COVID-19 vaccine starting August 13, 2021. This includes people who received booster doses and people who received additional doses.

Source: Immunization Data Lake. **Data as of November 16, 2021, 0600AM.**

Implementation of COVID-19 vaccine booster doses

- At least **31 million** individuals in the United States have received a COVID-19 vaccine booster dose
- **~17 million** individuals ≥65 years of age received a COVID-19 booster dose
- Some states currently broadening booster eligibility criteria

Implementation of COVID-19 vaccine booster doses

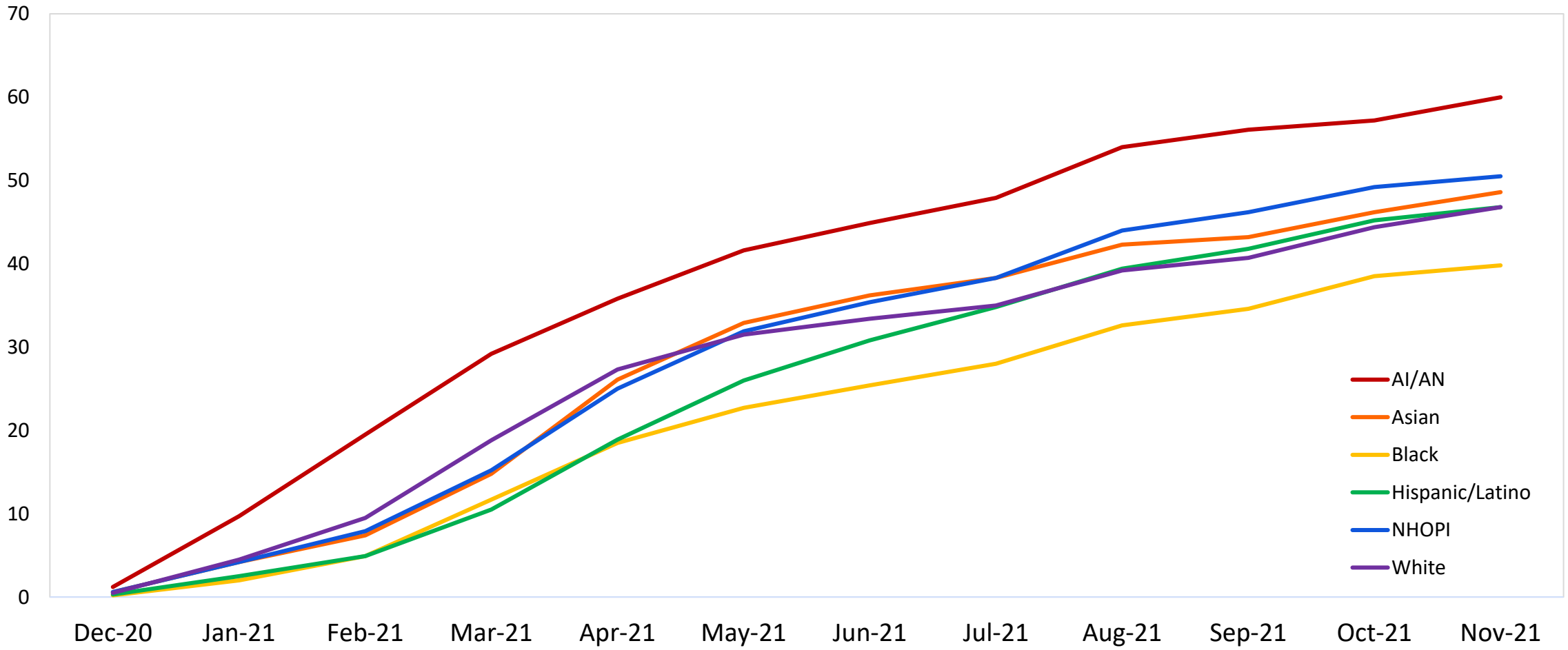
Considerations

- Vaccine recommendations based on risk and exposures are more difficult to implement than age-based recommendations
- ACIP recommendations that are **consistent** with the FDA EUA are easier to communicate and implement
- If recommendations for booster doses varied across the two mRNA vaccines, it would be difficult to communicate and implement

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

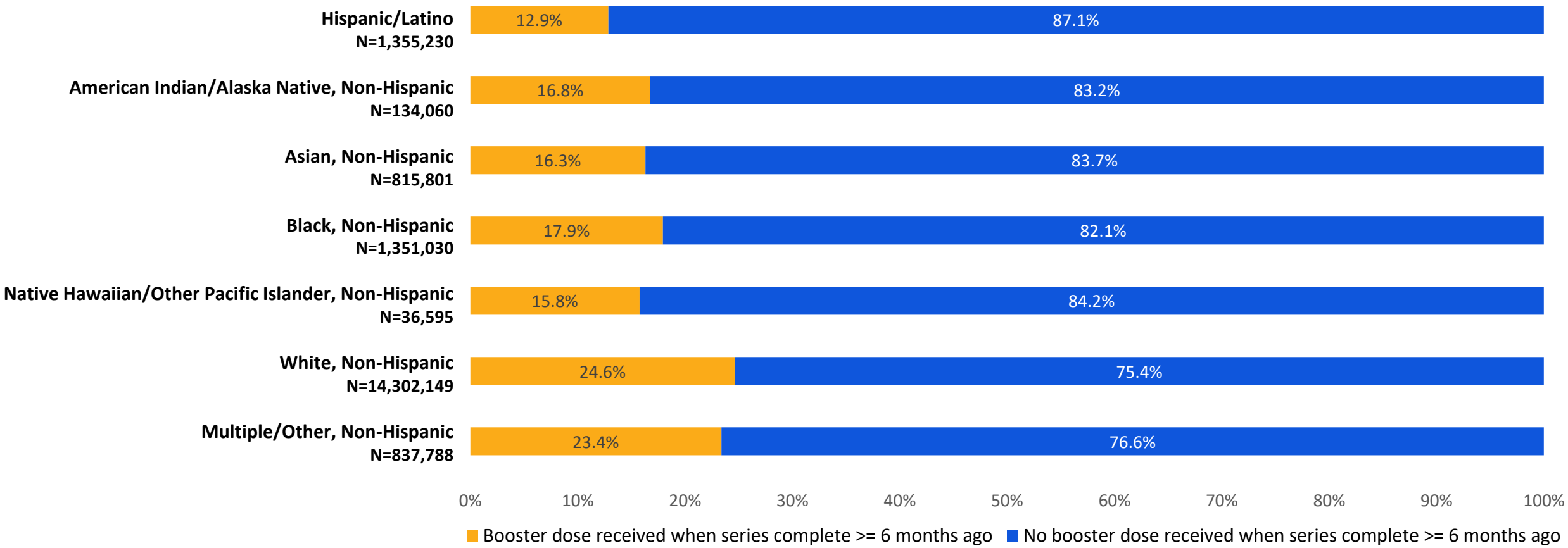
Percentage of people who have received at least one dose of the COVID-19 vaccine by race/ethnicity over time



CDC. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends as of November 16, 2021, and US Census Bureau National Population Estimates

Booster doses in persons ≥18 years of age with completed vaccination series ≥6 months earlier* by race/ethnicity

Data from **27,085,156** people with booster doses
Race/ethnicity was available for **18,832,653 (69.5%)** people with a booster dose



Notes: *Includes Janssen booster doses for people who have completed a primary vaccination series >= 2 months earlier. Number of people who received a booster dose includes anyone who is fully vaccinated and has received another dose of COVID-19 vaccine starting August 13, 2021. This includes people who received booster doses and people who received additional doses. The expected timing for a booster dose was set at >=6 months after primary series completion. Primary series is determined by the vaccine type of the second mRNA dose received or the first J&J/Janssen dose received. Does not include vaccine administrations reported by Texas as the primary series cannot be linked to booster dose in the aggregate format submitted by Texas. **Source:** Immunization Data Lake. Data as of November 16, 2021, 0600AM.

Summary - Equity

- Some disparities in primary series vaccine delivery have improved over time
- Early data on COVID-19 booster doses demonstrates disparities by race and ethnicity
  - Recommendations that are complex, difficult to communicate, or difficult to implement may worsen disparities in booster vaccination rates

Summary


DEPARTMENT OF HEALTH & HUMAN SERVICES USA
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Work Group Interpretation

- **Top priority** should be **continued vaccination** of **unvaccinated individuals**
- Balance of benefits and risks **varies by age**
  - Older adults have the clearest benefit/risk balance
  - Myocarditis data after booster doses reassuring to date, continue to closely monitor
  - Increases in COVID-19 cases may also impact benefit/risk balance

Goals of COVID-19 vaccines:

- Primary goal: Prevention of **severe disease**
- Secondary goals:
  Maintaining workforce and healthcare capacity
  Reduce infection and transmission
- Unknown impact of COVID-19 vaccine booster dose on prevention of transmission. However, even reduction in transmission may be important around winter and holidays

Evidence to Recommendations Framework

Type of recommendation	We do not recommend the intervention	We recommend the intervention for individuals based on assessment of **benefits** and **risks**	We recommend the intervention

Used when the **risks** clearly outweigh the **benefits**

Used when there is <u>diversity</u> of the **benefits** and **risks**

Can allow <u>flexibility</u> across a population

Used when the **benefits** clearly outweigh the **risks**

Evidence to Recommendations Framework

Type of recommendation	We do not recommend the intervention	We recommend the intervention for individuals based on assessment of **benefits** and **risks**	We recommend the intervention

Used when the **risks** clearly outweigh the **benefits**

Used when there is <u>diversity</u> of the **benefits** and **risks**

Can allow <u>flexibility</u> across a population

<u>MAY</u> receive a booster

Used when the **benefits** clearly outweigh the **risks**

<u>SHOULD</u> receive a booster

Individual benefit-risk considerations for people who may receive a booster dose

- Potential **benefits** of booster dose
  - Reduced risk of SARS-CoV-2 infection, severe disease
  - May reduce transmission of SARS-CoV-2 to others
- Potential **risks** of booster dose
  - Rare risks of serious adverse events (e.g., myocarditis, pericarditis, TTS, GBS, anaphylaxis)
  - Common risks of transient local and systemic symptoms
- **Individual risk factors** for SARS-CoV-2 infection
  - Risk of exposure (occupational and institutional settings, e.g., healthcare workers, long term care settings)
  - Risk for infection (time since completion of primary series)
- **Individual impacts** of SARS-CoV-2 infection
  - Risk for severe infection (related to underlying conditions)
  - Risk associated with a person's circumstances (living with/caring for at-risk individuals or consequences of inability to meet obligations due to infection)

CDC https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Updates for the future

- Updates from a Moderna COVID-19 booster dose
- Rates of myocarditis after 3rd dose
- Updated data for overall safety profile of booster doses
- Continued evaluations for vaccine effectiveness
  - Includes VE for primary series and booster doses

Current recommendations for booster doses of COVID-19 vaccines

<table>
<tr><th rowspan="2">Age</th><th colspan="4">mRNA COVID-19 vaccine primary series</th><th rowspan="2">Janssen COVID-19 vaccine primary series</th></tr>
<tr><th>No risk factors</th><th>Occupational or institutional exposures</th><th>Underlying medical conditions</th><th>Resident of LTCF</th></tr>
<tr><td>≥65 years</td><td colspan="3">Should
receive a booster</td><td rowspan="3">Should
receive a booster</td><td rowspan="3">Should
receive a booster</td></tr>
<tr><td>50–64 years</td><td rowspan="2">Not eligible</td><td rowspan="2">May
receive a booster</td><td>Should
receive a booster</td></tr>
<tr><td>18–49 years</td><td>May
receive a booster</td></tr>
</table>

Proposed recommendations for booster doses of COVID-19 vaccines

<table>
<tr><th rowspan="2">Age</th><th colspan="3">mRNA COVID-19 vaccine primary series</th><th rowspan="2">Janssen COVID-19 vaccine primary series</th></tr>
<tr><th>No risk factors</th><th>Underlying medical conditions</th><th>Resident of LTCF</th></tr>
<tr><td>≥65 years</td><td>Should receive a booster</td><td rowspan="2">Should receive a booster</td><td rowspan="3">Should receive a booster</td><td rowspan="3">Should receive a booster</td></tr>
<tr><td>50–64 years</td><td rowspan="2">May receive a booster</td></tr>
<tr><td>18–49 years</td><td>May receive a booster</td></tr>
</table>

Policy Question

- Do the balance of benefits and risks and facilitation of implementation warrant an update to COVID-19 vaccine policy?

All other persons ≥18 years of age **may receive** a COVID-19 booster dose ≥6 months after completion of the mRNA primary series under the current Emergency Use Authorization

Persons who should receive a COVID-19 booster dose

- Aged ≥65 years
- Aged ≥18 years and reside in long-term care settings
- Aged 50-64 years with certain underlying medical conditions

Persons who may receive a COVID-19 booster dose, based on individual benefits and risks

- All other persons aged ≥18 years

Proposed recommendations for booster doses of COVID-19 vaccines

Option #2

Age	mRNA COVID-19 vaccine primary series		Janssen COVID-19 vaccine primary series
	No risk factors	Resident of LTCF	
≥65 years	**Should** receive a booster	**Should** receive a booster	**Should** receive a booster
50–64 years			
18–49 years	**May** receive a booster		

COVID-19 vaccine booster dose in persons who completed an mRNA primary series: PROPOSED, Option #2

Persons who <u>should</u> receive a COVID-19 booster dose

Aged ≥50 years

Aged ≥18 years residing in LTCF

Persons who <u>may</u> receive a COVID-19 booster dose, based on individual benefits and risks

All other persons aged ≥18 years

- Booster dose administered at least 6 months after completion of primary series
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

ACIP Vote
Interim Recommendation

A single COVID-19 vaccine booster dose is recommended for persons aged **≥18 years*** who received an mRNA COVID-19 vaccine primary series based on **individual benefit and risk,** at least 6 months after the primary series, under the FDA's Emergency Use Authorization

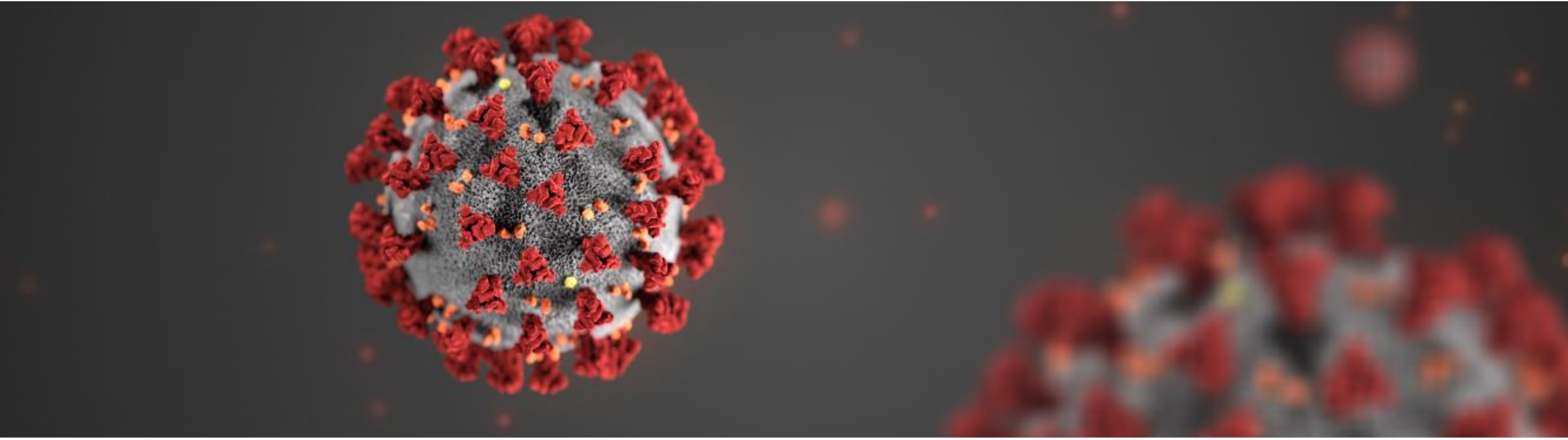
*Individuals ≥18 years of age not otherwise recommended to receive a COVID-19 vaccine

ACIP Vote
Interim Recommendation
Option #2

A single COVID-19 vaccine booster dose is recommended for persons aged **≥50 years** who received an mRNA COVID-19 vaccine, at least 6 months after the primary series, under the FDA's Emergency Use Authorization

Acknowledgments

- Monica Godfrey
- Megan Wallace
- Sarah Mbaeyi
- Rachel Gorowitz
- Jack Gersten
- Jefferson Jones
- Eddie Shanley
- Mary Chamberland
- Deblina Datta
- Stephen Hadler
- VTF ACIP WG Team
- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Respiratory Viruses Branch



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

COVID-19 vaccine booster dose in persons who completed an mRNA primary series: PROPOSED

Persons who <u>should</u> receive a COVID-19 booster dose

- Aged ≥65 years
- Aged ≥18 years and reside in long-term care settings
- Aged 50-64 years with certain underlying medical conditions

Persons who <u>may</u> receive a COVID-19 booster dose, based on individual benefits and risks

- All other persons aged ≥18 years

- Booster dose administered at least 6 months after completion of primary series
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

Policy Question

Adults ≥50 years of age should receive a COVID-19 vaccine booster dose

PROS	CONS
• Age based recommendations are easier to communicate • Current inclusive list of 'underlying medical conditions' likely includes ~75% of those 50-64 years of age • Inclusive list of 'underlying medical conditions' can be difficult for providers to identify those at risk • Lowest risk of myocarditis after mRNA vaccines in this age group, impacting the balance of benefits/risks • Adults 50-64 years of age, even those without medical conditions, may be at increased risk of severe COVID-19	• Limited VE data to specifically compare those 50-64 years with and without underlying medical conditions • Risk of rare adverse events

Proposed recommendations for booster doses of COVID-19 vaccines

Individuals who <u>should</u> get a booster

≥18 years
who received a Janssen/J&J COVID-19 vaccine

≥65 years
who received an mRNA COVID-19 vaccine

50-64 years with underlying medical conditions
who received an mRNA COVID-19 vaccine

≥18 years residing in LTCF
who received an mRNA COVID-19 vaccine

Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

Individuals who <u>may</u> get a booster

Other persons ≥18 years
who received an mRNA COVID-19 vaccine

Current recommendations for booster doses of COVID-19 vaccines

<table>
<tr><th>Age</th><th>With Underlying Medical Conditions</th><th>mRNA COVID-19 vaccine primary series</th><th>Janssen COVID-19 vaccine primary series</th><th>Residents of LTCF</th></tr>
<tr><td>≥65 years</td><td></td><td rowspan="2">Should
receive a booster</td><td rowspan="4">Should
receive a booster</td><td rowspan="4">Should
receive a booster</td></tr>
<tr><td rowspan="2">50–64 years</td><td>With conditions</td></tr>
<tr><td>Without conditions</td><td>May receive a booster if institutional/ occupational exposure</td></tr>
<tr><td rowspan="2">18–49 years</td><td>With conditions</td><td>May
receive a booster</td></tr>
<tr><td>Without conditions</td><td>May receive a booster if institutional/ occupational exposure</td></tr>
</table>

Populations who should receive a booster dose

No proposed changes

Individuals:
≥18 years

Primary Series

Janssen/J&J
COVID-19
vaccine

At least
2 months

Booster Dose

Janssen/J&J
COVID-19
vaccine

mRNA COVID-19
vaccine

Populations who should receive a booster dose

No proposed changes

Individuals:
≥65 years of age
≥18 years residing in LTCF
50-64 years with underlying medical conditions

mRNA COVID-19 vaccine

At least **6 months**

Janssen/J&J COVID-19 vaccine

mRNA COVID-19 vaccine

Primary Series

Booster Dose

Populations who may receive a booster dose: Current

Individuals:
18-49 years with underlying medical conditions
18-64 years at increased risk
due to occupational/institutional setting

mRNA COVID-19 vaccine

At least **6 months**

Janssen/J&J COVID-19 vaccine

mRNA COVID-19 vaccine

Primary Series

Booster Dose

Populations who may receive a booster dose: Proposed

All other persons
≥18 years

mRNA COVID-19 vaccine

At least
6 months

Janssen/J&J COVID-19 vaccine

mRNA COVID-19 vaccine

Primary Series

Booster Dose

Policy Question #1

Adults ≥65 years of age and LTCF residents

PROS	CONS
• Highest risk of severe disease • Largest impact in waning VE against severe disease • Prioritized for early doses of COVID-19 vaccines (longer duration since primary series)	Age cut-off may not represent continuum of risk

Policy Question #2

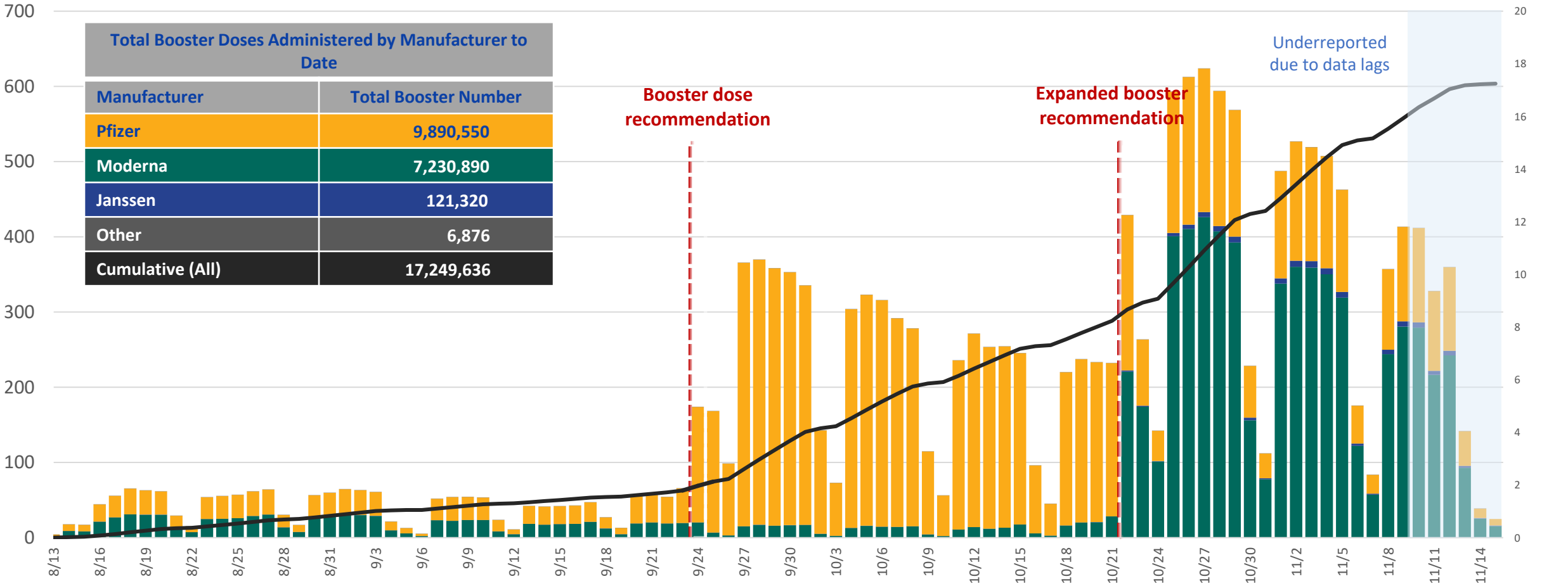
Adults 18–64 years of age at risk for severe COVID-19 due to **underlying medical conditions** or at risk of SARS-CoV-2 exposure due to **occupation/setting**

Type of recommendation	PROS	CONS
Standard recommendation	• Simple • Reduces barriers for individuals who may have increased risk of disease • Reduction in infection could reduce work absenteeism	• Not strong evidence of increased risk of hospitalization or death in all individuals • Balance of benefits and risks likely varies • Large number of people initially eligible (>50 million)
Recommended for individuals based on assessment of benefits and risks	• Reduces barriers for individuals who may have increased risk of disease • Reduction in infection could reduce work absenteeism • Reflects uncertainty in current balance of benefits and risks in this population	• Large number of people initially eligible (>50 million) • More complicated to implement

Daily number of booster doses administered, by manufacturer

Persons ≥65 years of age

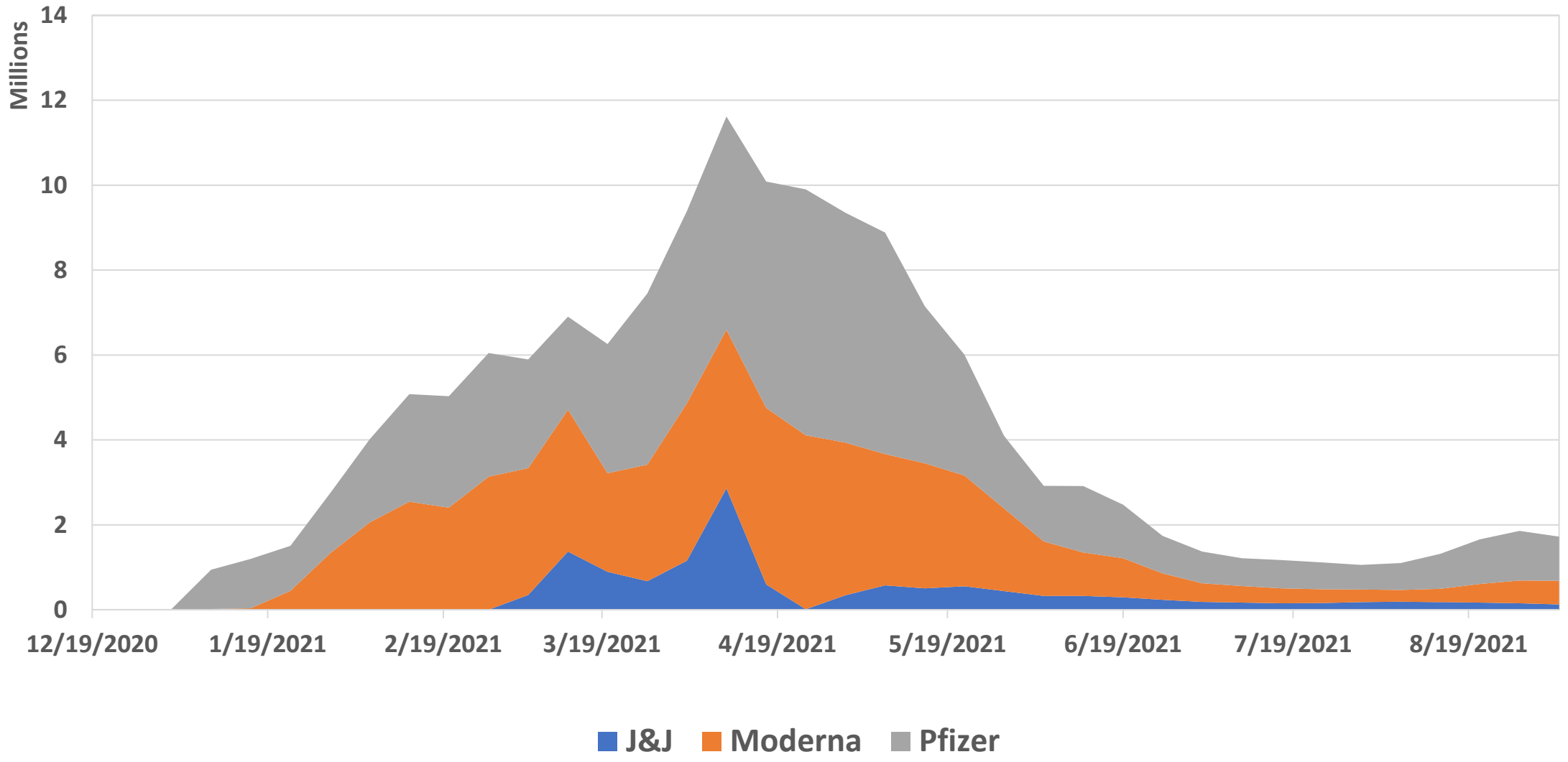
Total Booster Doses Administered by Manufacturer to Date	
Manufacturer	Total Booster Number
Pfizer	9,890,550
Moderna	7,230,890
Janssen	121,320
Other	6,876
Cumulative (All)	17,249,636



Note: Number of people who received a booster dose includes anyone who is fully vaccinated and has received another dose of COVID-19 vaccine starting August 13, 2021. This includes people who received booster doses and people who received additional doses.

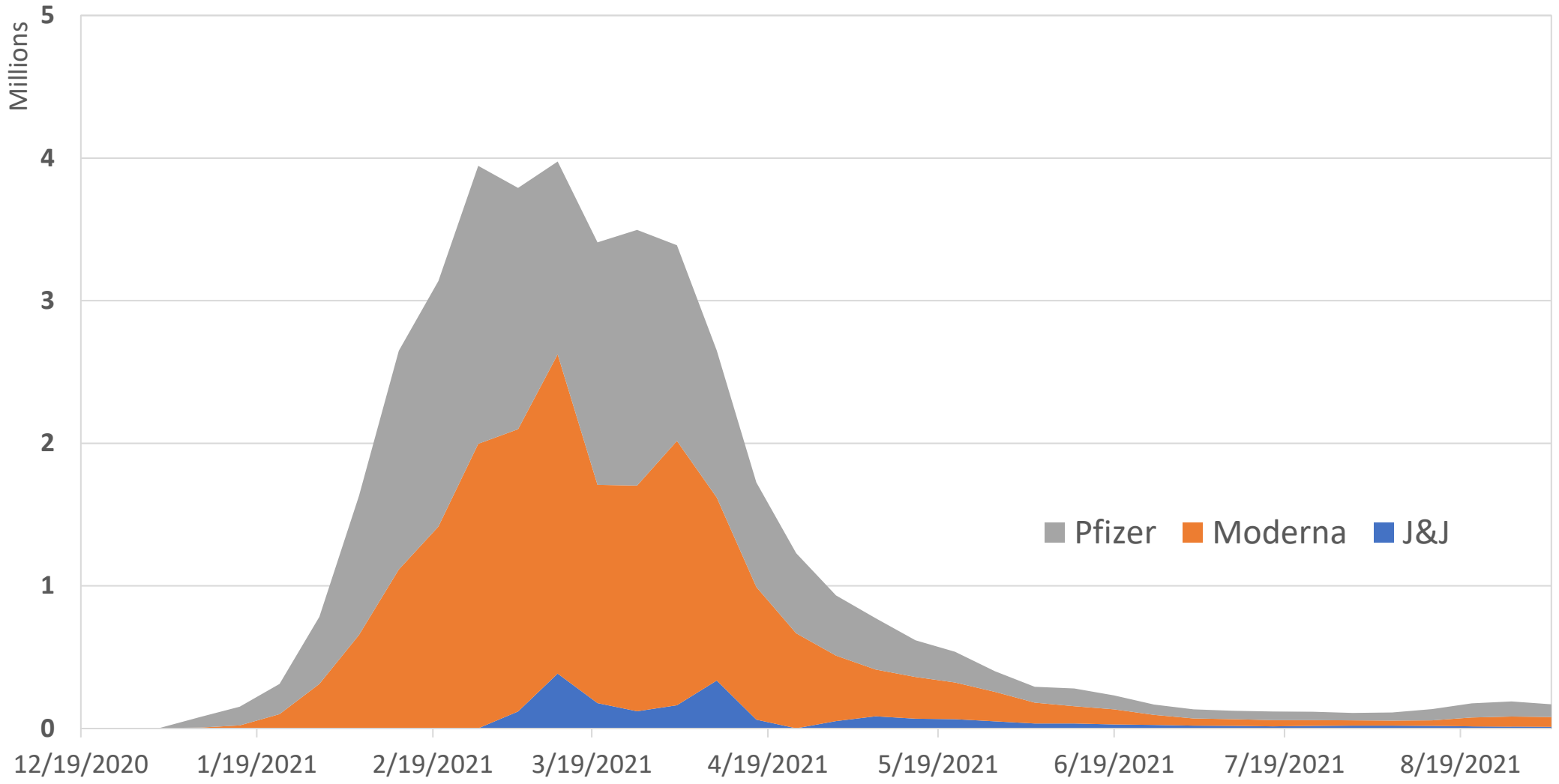
Source: Immunization Data Lake. **Data as of November 16, 2021, 0600AM.**

Completed primary vaccination series by week



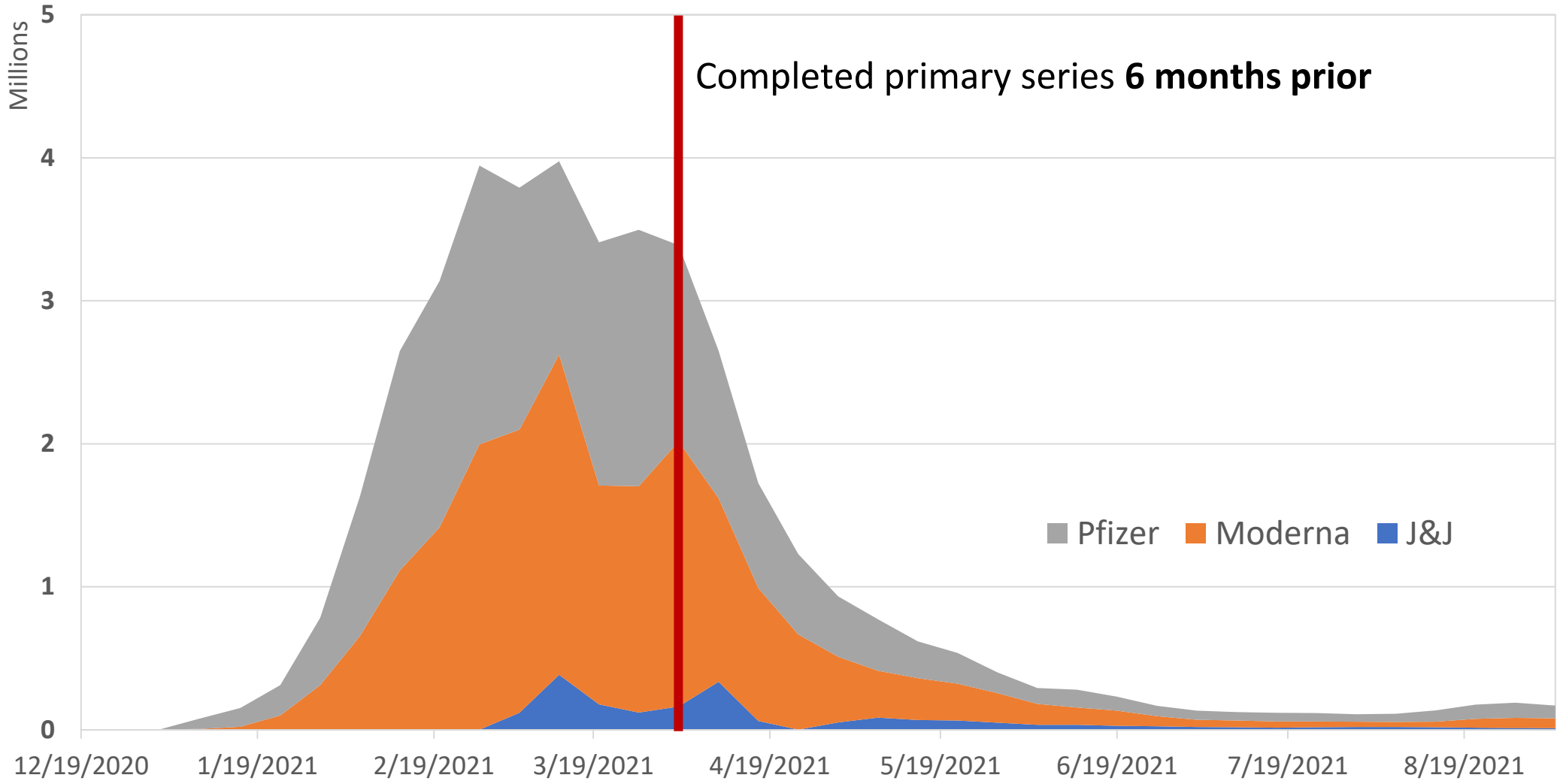
Completed primary vaccination series by week:

Adults ≥65 years of age

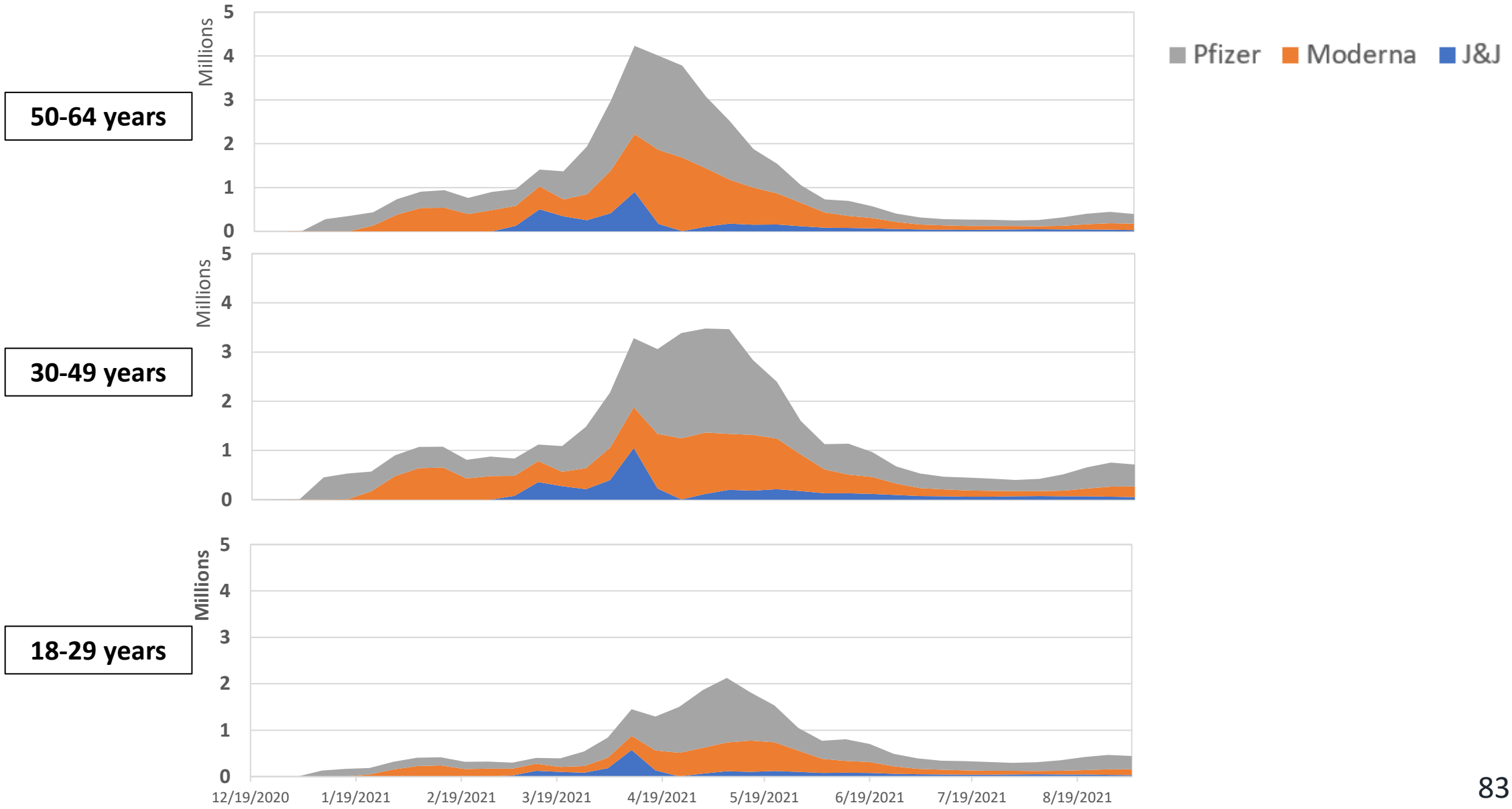


Completed primary vaccination series by week:

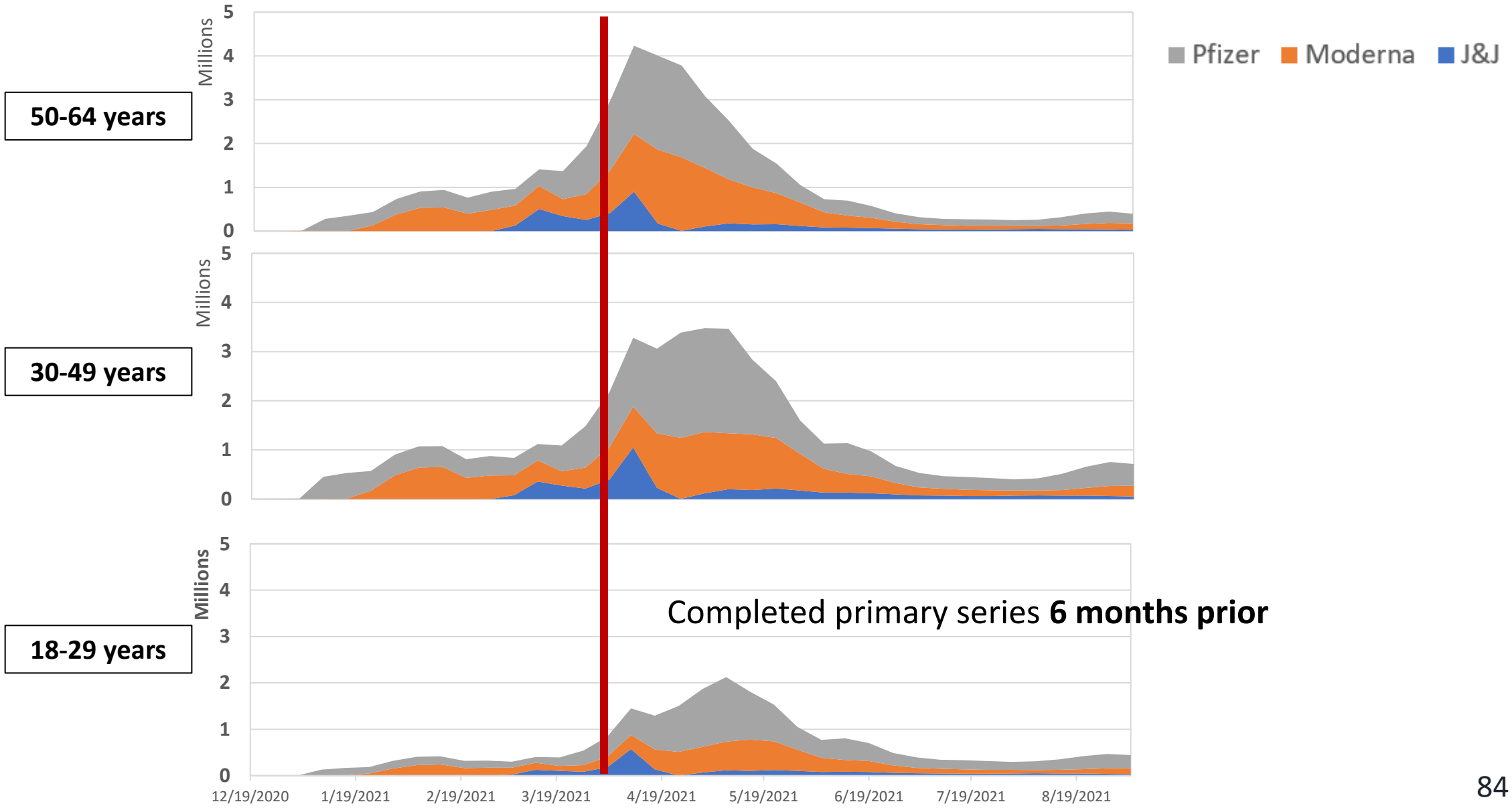
Adults ≥65 years of age



Completed primary vaccination series by week and age



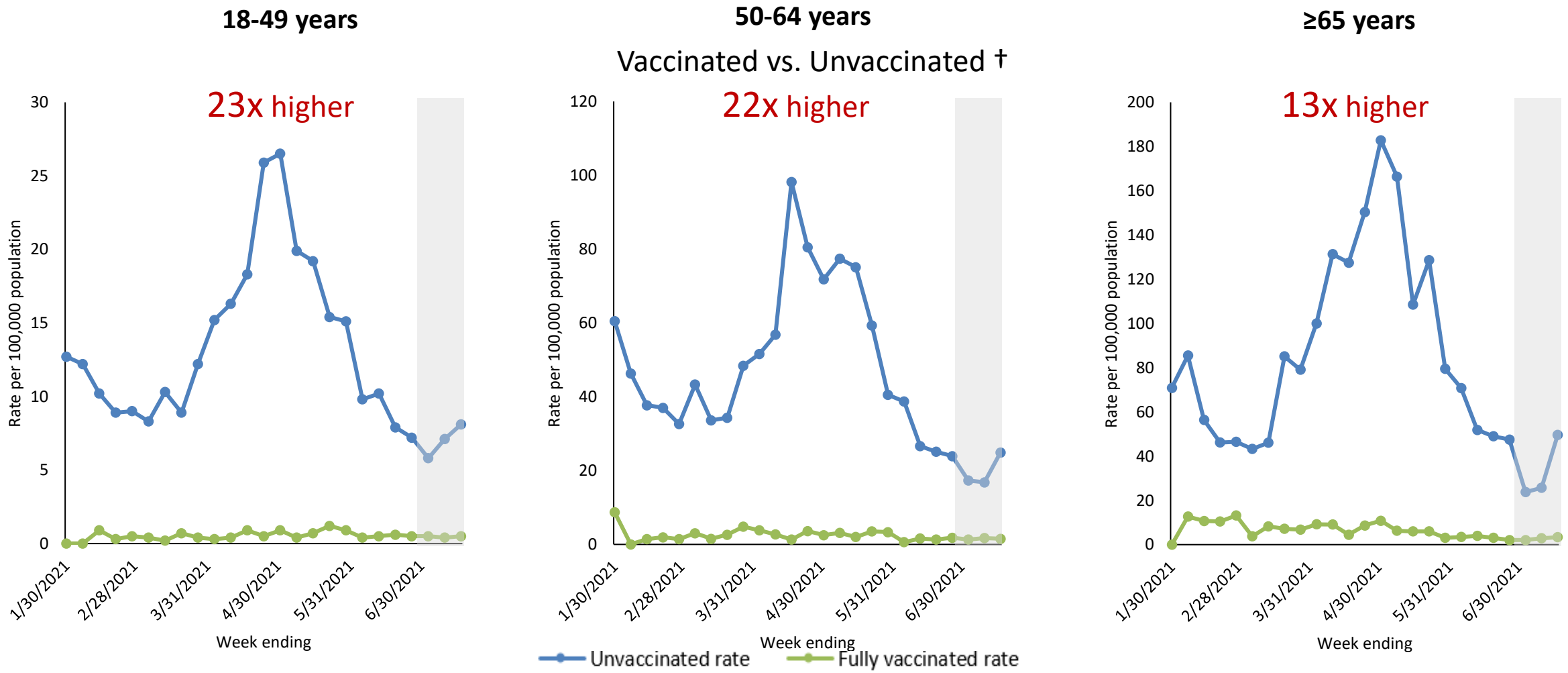
Completed primary vaccination series by week and age



Number of persons eligible (in millions) for a booster dose on September 27th, 2021

	≥6 months after primary series			
Age group	**Pfizer-BioNTech**	**Moderna**	**Janssen/J&J**	**Total**
18-29 years old	2.0	1.5	0.3	**3.9**
30-49 years old	5.5	4.4	0.9	**10.8**
50-64 years old	5.3	4.4	1.2	**11.0**
65+ years old	13.6	12.9	0.8	**27.4**
Total	**26.4**	**23.4**	**3.3**	**53.0**

Age-adjusted weekly COVID-19-associated hospitalization rates among adults by week of admission and age group*—COVID-NET, January 24–July 17, 2021



*Data are preliminary and case counts and rates for recent hospital admissions are subject to lag. As data are received each week, prior case counts and rates are updated accordingly.
†Cumulative rate ratio from January 24 – July 17, 2021. Shaded area indicates preliminary July data that does not include one site.
Havers et al. https://medrxiv.org/cgi/content/short/2021.08.27.21262356v1. COVID-19-associated hospitalizations among vaccinated and unvaccinated adults ≥18 years - COVID-NET, 13 states, January 1-July 24, 2021

Policy Options

	ACIP **recommends** the intervention	ACIP **recommends** for individuals based on assessment of benefit and risk
Option #1	≥65 years of age and LTCF residents	None
Option #2	≥65 years of age and LTCF residents	Individuals 18-64 years of age *at risk of severe COVID-19 due to* ***occupation/setting*** *or* ***underlying medical conditions***
Option #3	≥65 years of age **-AND-** Individuals ≥18 years of age *at risk for COVID-19 due to* ***occupation/setting*** *or* ***underlying medical conditions***	None

Number of persons ≥65 years eligible (in millions) for a booster by week

	≥6 months after primary series			
Week of	Pfizer-BioNTech	Moderna	Janssen/J&J	Total
Sept 27	13.6	12.9	0.8	**26.5**
Oct 4	1.4	1.9	0.2	**3.3**
Oct 11	1	1.3	0.3	**2.3**
Oct 18	0.7	0.9	0.1	**1.6**
Oct 25	0.6	0.7	0	**1.3**
Nov 1	0.4	0.5	0.1	**0.9**
Nov 8	0.4	0.3	0.1	**0.7**

Number of persons 18-64 eligible (in millions) for a booster by week

	≥6 months after primary series			
Week of	Pfizer-BioNTech	Moderna	Janssen/J&J	Total
Sept 27	12.8	10.4	2.5	**25.7**
Oct 4	3.2	1.9	1.0	**3.3**
Oct 11	4.0	2.5	2.5	**2.3**
Oct 18	4.6	3.2	0.5	**1.6**
Oct 25	5.2	3.4	0	**1.3**
Nov 1	5.0	3.1	0.3	**0.9**
Nov 8	4.9	2.8	0.5	**0.7**

Jurisdictional survey of readiness for booster doses (n=57)

- **54%** of jurisdictions state they have taken significant action to estimate potential demand and needed supply for booster doses
- **51%** of jurisdictions state they have taken some action to communicate with providers around booster dose expectations including scheduling, clinical guidance and co-administration
- **45%** of jurisdictions state their system does not allow easy access for immunization records, if needed for booster doses
  - Could be relevant if individuals do not remember the type of vaccine received for primary dose

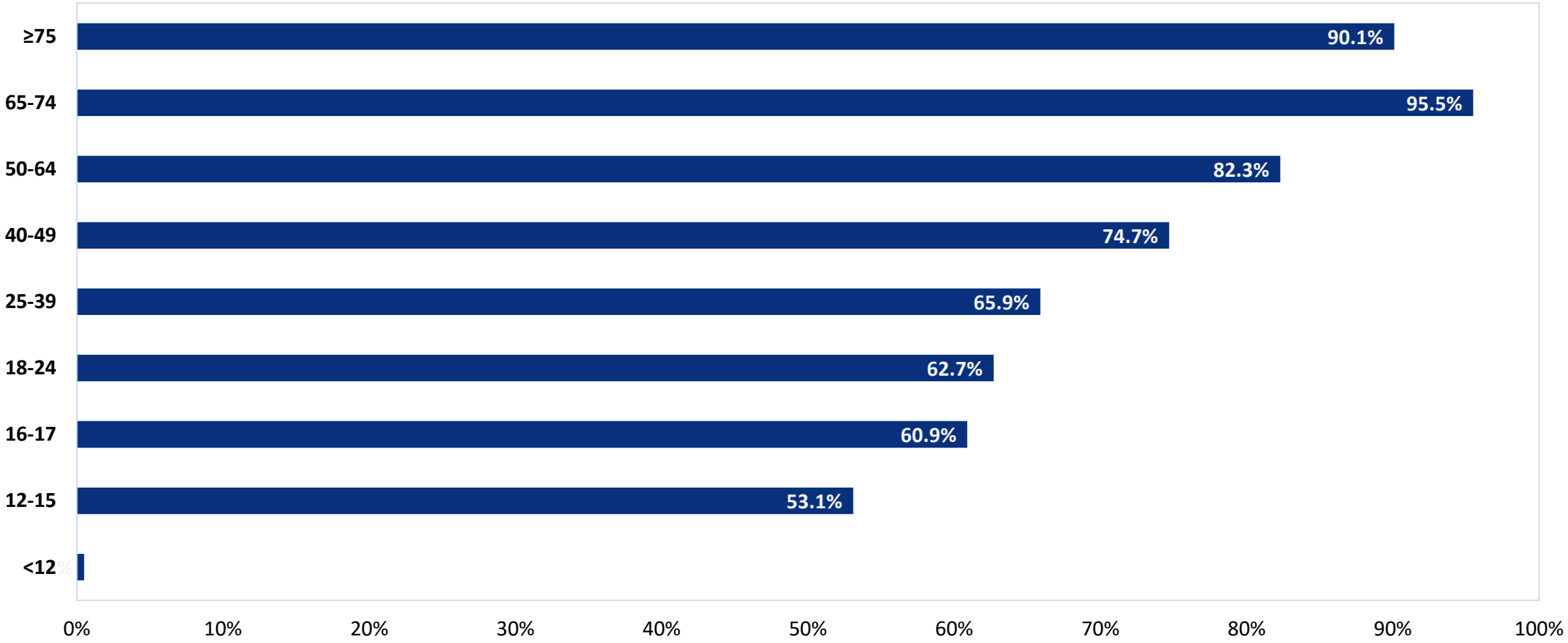
CAG. Jurisdictional Readiness for Booster Doses Survey unpublished data, September 2021

COVID-19 vaccine administration fees

- All organizations and providers participating in the CDC COVID-19 Vaccination Program:
  - **must** administer COVID-19 Vaccine at no out-of-pocket cost to the recipient
  - may **not** deny anyone vaccination based on the vaccine recipient's coverage status or network status
  - may **not** charge an office visit or other fee if COVID-19 vaccination is the sole medical service provided
  - may **not** require additional medical services to receive COVID-19 vaccination
  - **may** seek appropriate reimbursement from a program or plan that covers COVID-19 Vaccine administration fees for the vaccine recipient, such as:
    - vaccine recipient's private insurance company
    - Medicare or Medicaid reimbursement
    - HRSA COVID-19 Coverage Assistance Fund for underinsured vaccine recipients
    - HRSA COVID-19 Uninsured Program for non-insured vaccine recipients
- may **not** seek any reimbursement from the vaccine recipient

COVID-19 Vaccination Provider Requirements and Support | CDC

What percentage of people in each age range received at least one dose of COVID-19 vaccine?



CDC. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends. Accessed September 21, 2021

Number of persons eligible (in millions) for a booster dose on September 27th, 2021

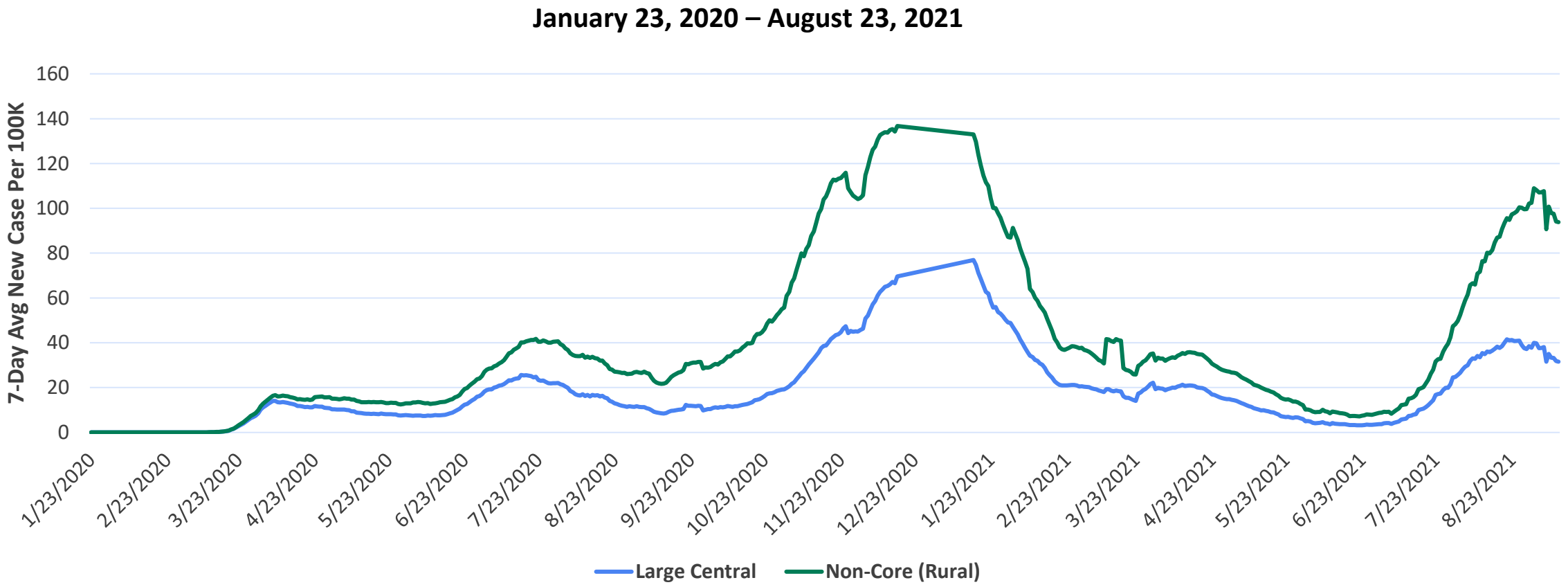
	6-month booster				8 month booster			
Age group	Pfizer	Moderna	J&J	Total	Pfizer	Moderna	J&J	Total
18-29 years old	2.0	1.5	0.3	**3.9**	0.6	0.2	--	**0.8**
30-49 years old	5.5	4.4	0.9	**10.8**	1.8	0.7	--	**2.5**
50-64 years old	5.3	4.4	1.2	**11.0**	1.3	0.5	--	**1.8**
65+ years old	13.6	12.9	0.8	**27.4**	0.9	0.4	--	**1.3**
Total	**26.4**	**23.4**	**3.3**	**53.0**	**4.6**	**1.8**	--	**6.5**

- With a **6 month interval**: >50 million individuals eligible; >27 million individuals ≥65 years of age
  - If recommendations are ONLY for recipients of Pfizer primary series: >25 million individuals, ~14 million ≥65 years of age
- With an **8 month interval**: >6 million individuals eligible; only 1 million individuals ≥65 years of age, and no Janssen recipients

Number of persons ≥65 years eligible (in millions) for a booster by week

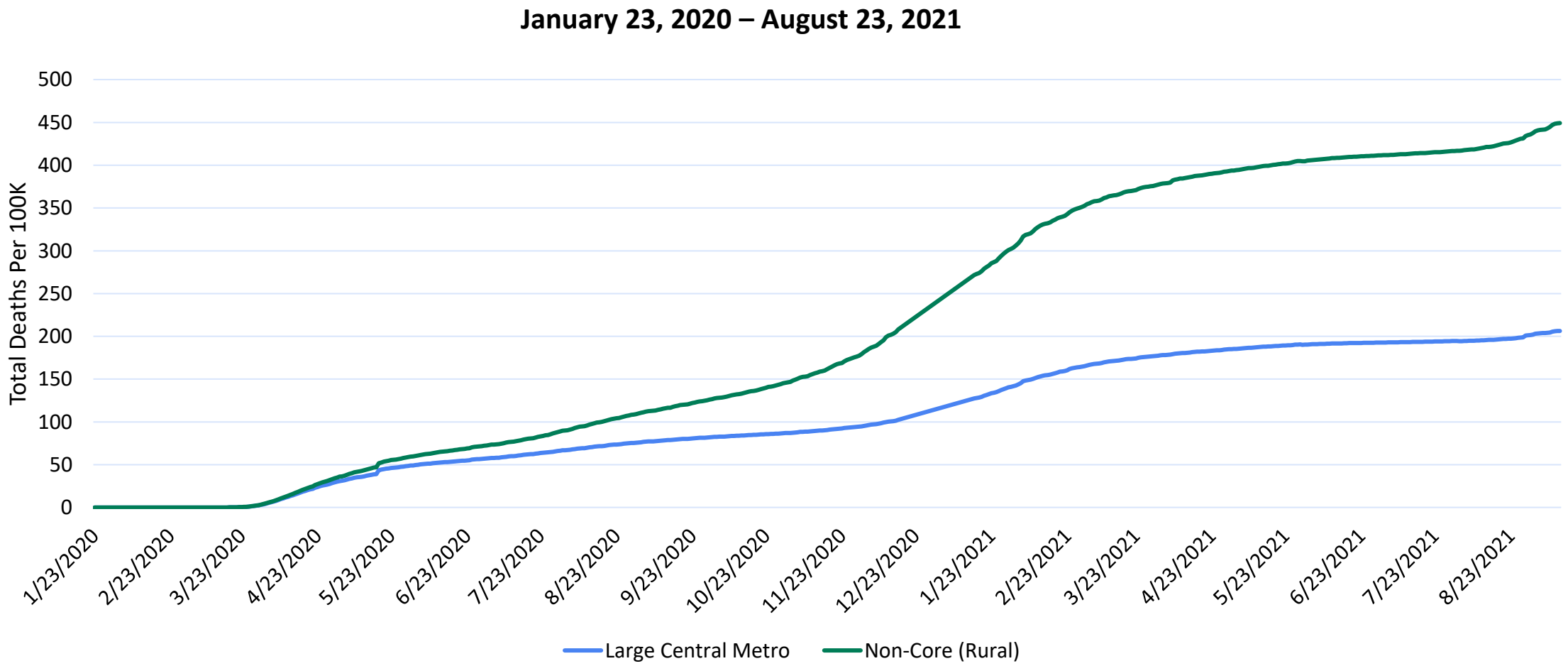
	6-month booster				8-month booster			
Week	Pfizer	Moderna	J&J	Total	Pfizer	Moderna	J&J	Total
9/27/2021	13.6	12.9	0.8	**26.5**	0.9	0.4	--	**1.3**
10/4/2021	1.4	1.9	0.2	**3.3**	1	0.7	--	**1.7**
10/11/2021	1	1.3	0.3	**2.3**	1.5	1.1	--	**2.6**
10/18/2021	0.7	0.9	0.1	**1.6**	1.7	1.4	--	**3.1**
10/25/2021	0.6	0.7	0	**1.3**	1.9	2	--	**3.9**
11/1/2021	0.4	0.5	0.1	**0.9**	1.7	2	0.1	**3.7**
11/8/2021	0.4	0.3	0.1	**0.7**	1.4	2.2	0.4	**3.6**

Equity: 7-Day Case Rate Per 100,000 Population in United States, by Urban/Rural Classification



CDC. https://covid.cdc.gov/covid-data-tracker/#pop-factors_7daynewcases. Accessed September 14, 2021.

Equity: COVID-19 Cumulative Death Rate Per 100,000 Population in United States, by County Urban/Rural Classification



CDC. https://covid.cdc.gov/covid-data-tracker/#pop-factors_totaldeaths. Accessed September 14, 2021.

35% of respondents who originally received a Janssen/J&J vaccine would want it again for a booster dose

51% of respondents who originally received an mRNA vaccine would want a Pfizer-BioNTech booster dose
31% of respondents who originally received an mRNA vaccine would want a Moderna booster dose

Janssen/J&J Booster Vaccine Concordance

mRNA Booster Vaccine Concordance

Prefer Janssen/J&J Booster

Prefer Pfizer-BioNTech Booster

Prefer Moderna Booster

No preference, unsure, or refused to answer

CDC/University of Iowa unpublished data, August 2021

Most vaccinated participants (76.1%) indicated that, if they receive a booster COVID-19 vaccine, they would like to receive an mRNA vaccine

CDC/University of Iowa unpublished data, August 2021

Hospitalized or fatal COVID-19 cases in vaccinated persons

- As of September 13, 2021, **more than 178 million** people in the United States had been fully vaccinated against COVID-19.

- During the same time, CDC received reports from 49 U.S. states and territories of **15,790** patients with COVID-19 and were hospitalized or died, who had been vaccinated.

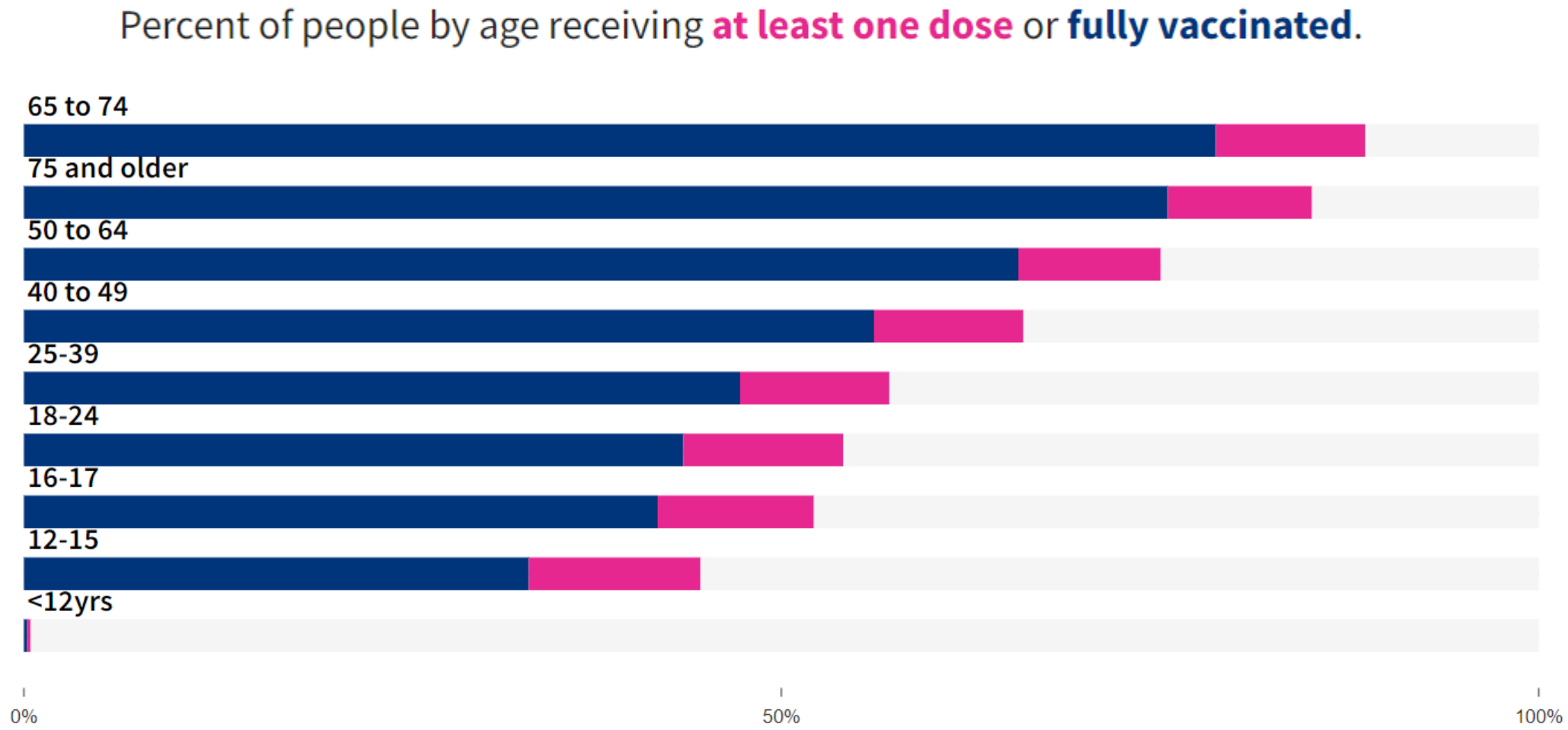
	Deaths		Hospitalized, non-fatal*	
Total	N=3,040		N=12,750	
Females	1,309	(43%)	6,100	(48%)
People aged ≥65 years	2,631	(87%)	8,902	(70%)
Asymptomatic or not COVID-related**	516	(17%)	2,562	(20%)

*This table separates all reported vaccine breakthrough infections that resulted in hospitalization and/or death into two columns. While most deaths were also among hospitalized individuals, a small number were not.

**Includes cases in which the patient did not have symptoms of COVID-19, or their hospitalization or death was not COVID-related. For example, people may be hospitalized for reasons other than COVID-19, such as an auto accident, and test positive when screened upon hospital admission.

CDC. https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html. Accessed September 19, 2021

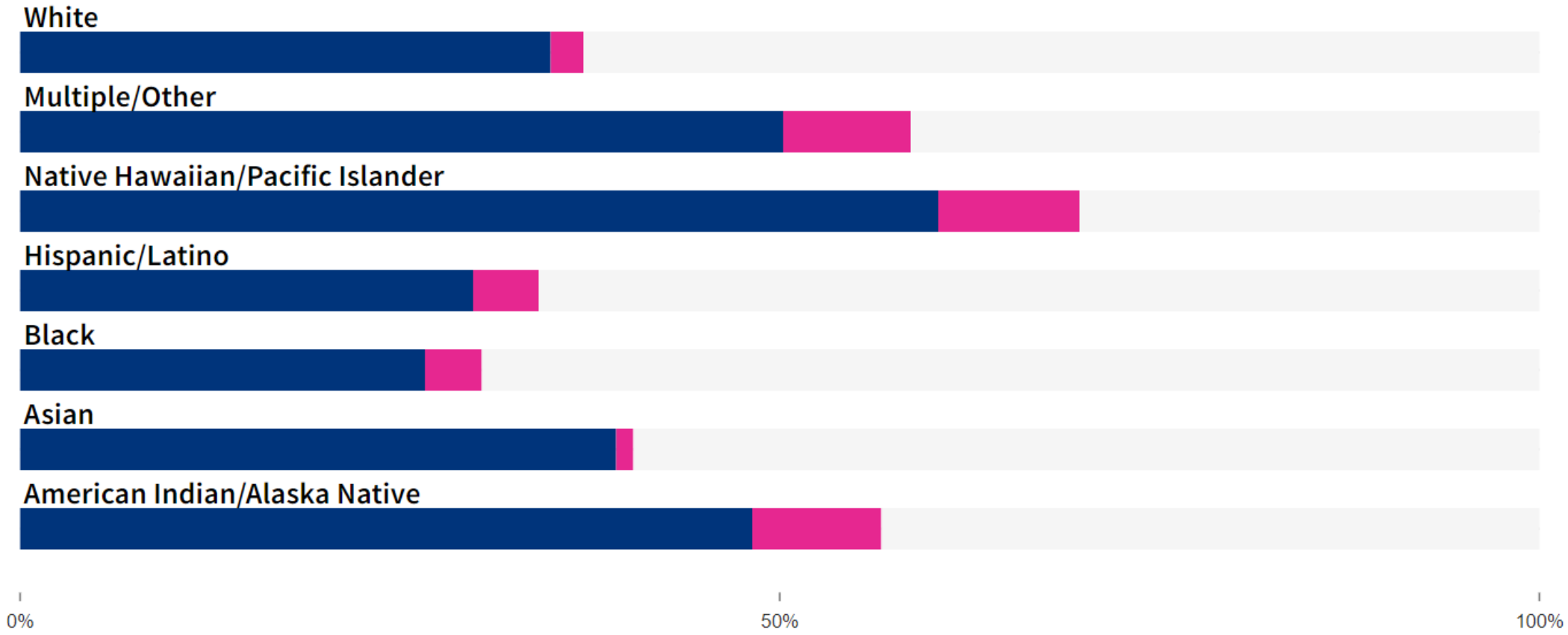
What percentage of people in each age range received the COVID-19 vaccine?



USA Facts. https://usafacts.org/visualizations/covid-vaccine-tracker-states. Accessed September 14, 2021

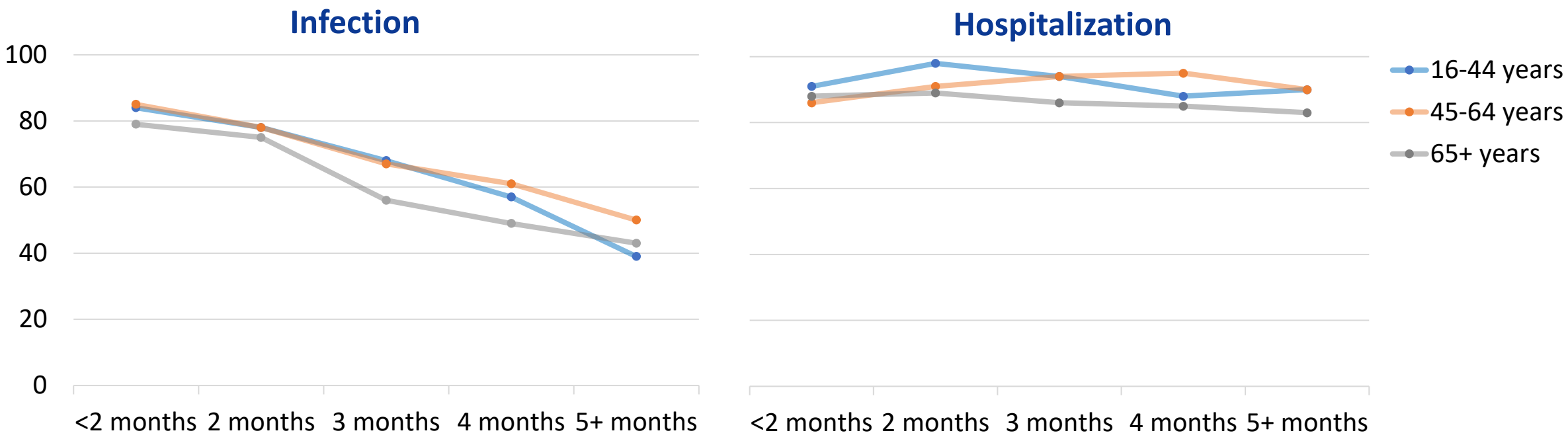
What percentage of people in each race or ethnic group received the COVID-19 vaccine?

According to the Centers for Disease Control and Prevention, there is race or ethnic information for **59%** of people who received **at least one dose** and **64%** of **fully vaccinated** people.



USA Facts. https://usafacts.org/visualizations/covid-vaccine-tracker-states. Accessed September 14, 2021.

Review of sponsor study of vaccine effectiveness (Tardof et al)



- Among fully vaccinated persons of all ages, protection against COVID-19-related hospitalization did not wane over time, with overall adjusted VE estimates of 87% (82–91) at < 1 month after being fully vaccinated, and 88% (82–92) at ≥5 months after full vaccination.
- Effectiveness against infection decreased over time among all ages, individuals ≥65 years of age had lower overall effectiveness against infections but declined at a similar rate

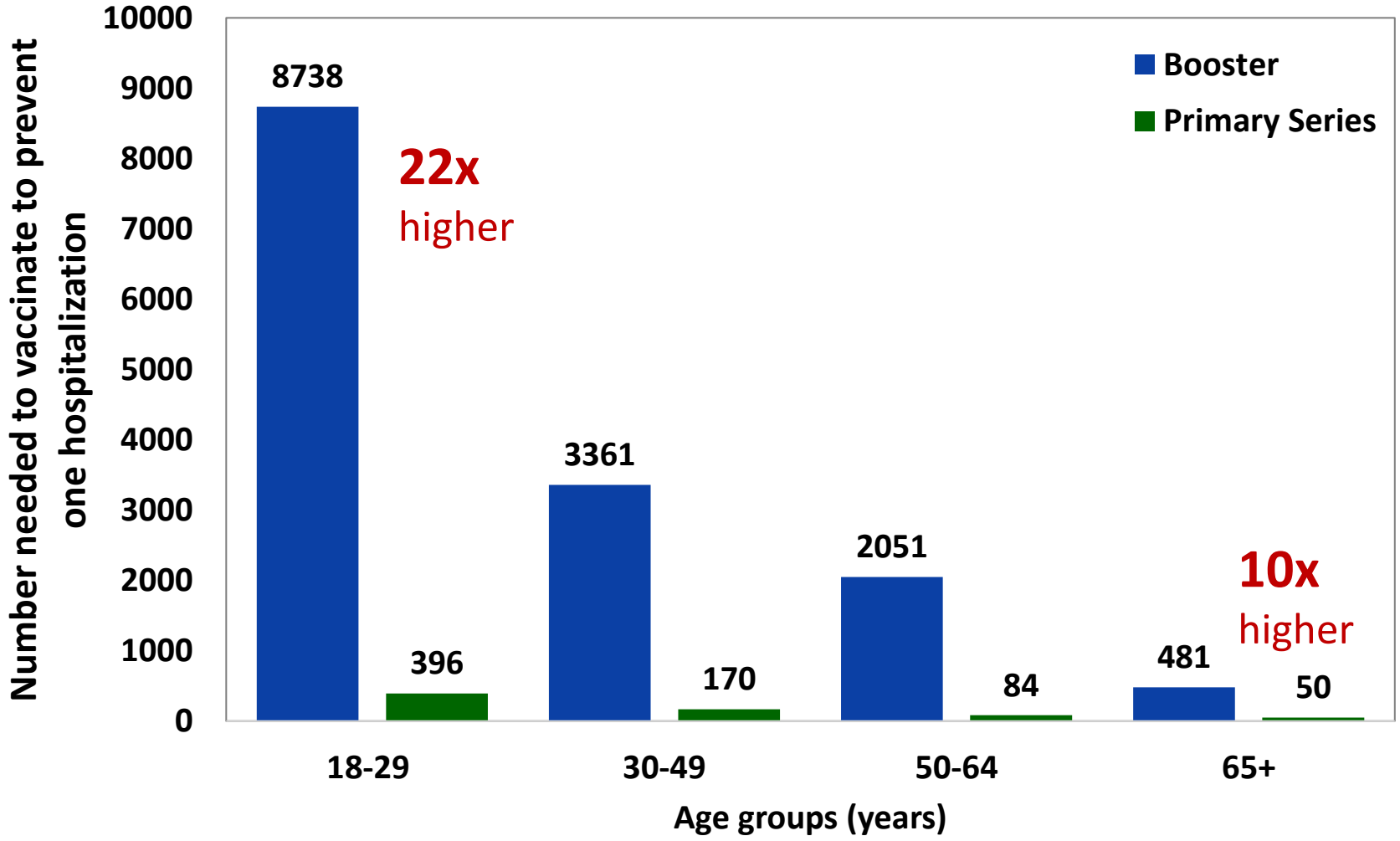
Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Six-month effectiveness of BNT162b2 mRNA COVID-19 vaccine in a large US integrated health system: a retrospective cohort study. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3909743

Booster vaccine type preferences by primary vaccination

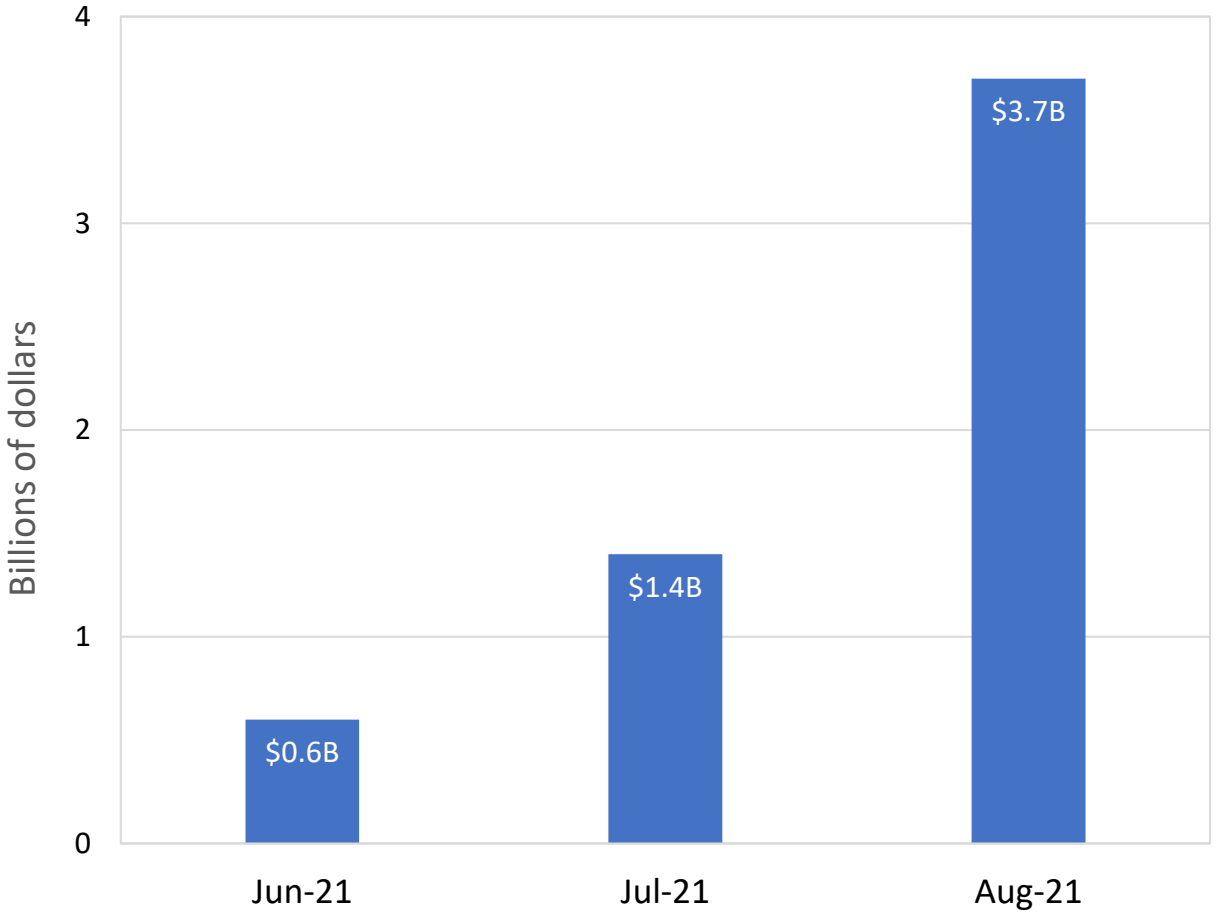
- Most vaccinated participants (**76.1%**) indicated that, if they receive a booster COVID-19 vaccine, they would like to receive an mRNA vaccine
- **51%** of respondents who originally received an mRNA vaccine would want a Pfizer-BioNTech booster dose
- **31%** of respondents who originally received an mRNA vaccine would want a Moderna booster dose
- **35%** of respondents who originally received a Janssen/J&J vaccine would want it again for a booster dose
- **10.9%** of vaccinated respondents expressed **no preference** in the type of COVID-19 booster

CDC/University of Iowa unpublished data, August 2021

Number needed to vaccinate to prevent one hospitalization over 6 months, booster versus primary series



Costs of unvaccinated COVID-19 hospitalizations to the U.S. health system, June – August 2021

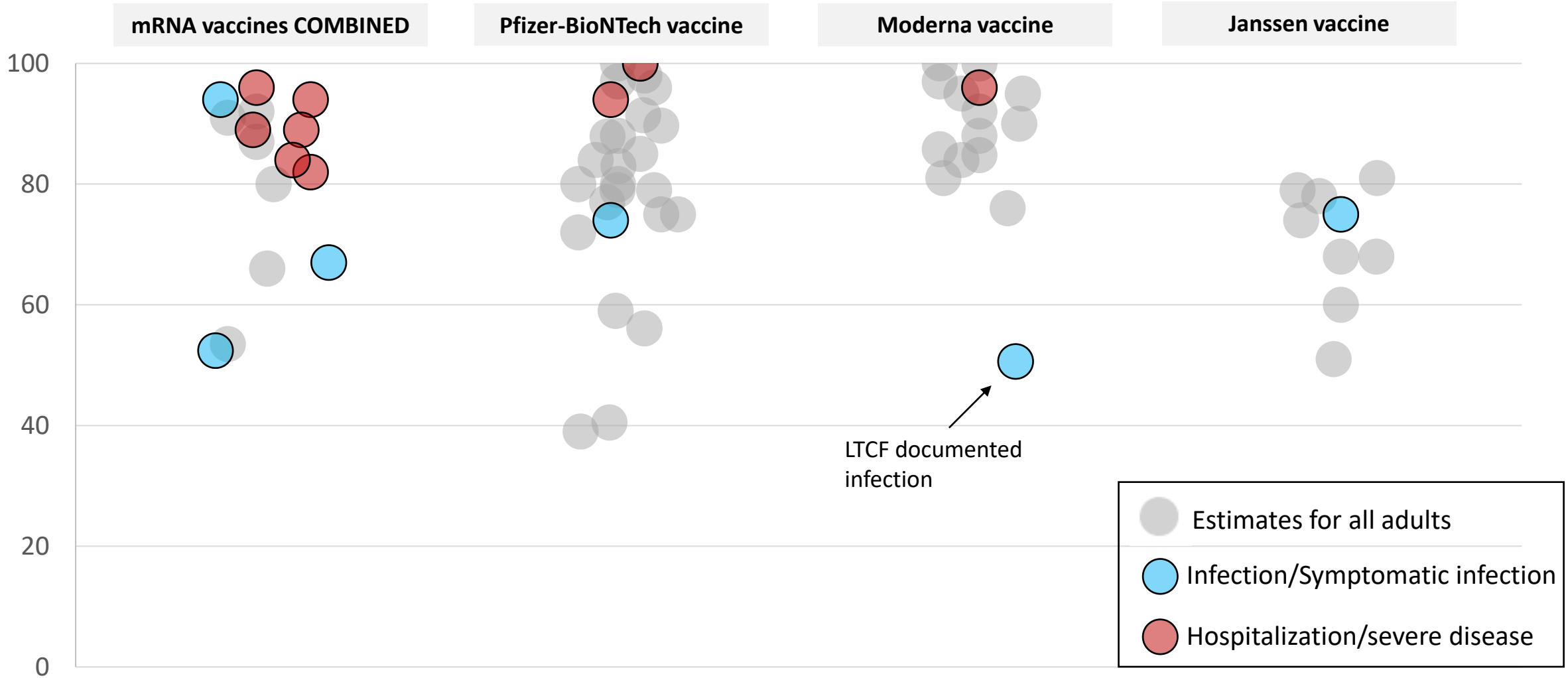


- Estimates over 280,000 (**84%**) of COVID-19 hospitalizations could have been prevented by vaccination
- The total preventable cost for unvaccinated COVID-related adult hospitalizations was **$5.7 billion**

Unvaccinated COVID-19 hospitalizations cost billions of dollars - Peterson-KFF Health System Tracker

Summary of **VE estimates** since introduction of the Delta variant

Adults ≥60 years of age

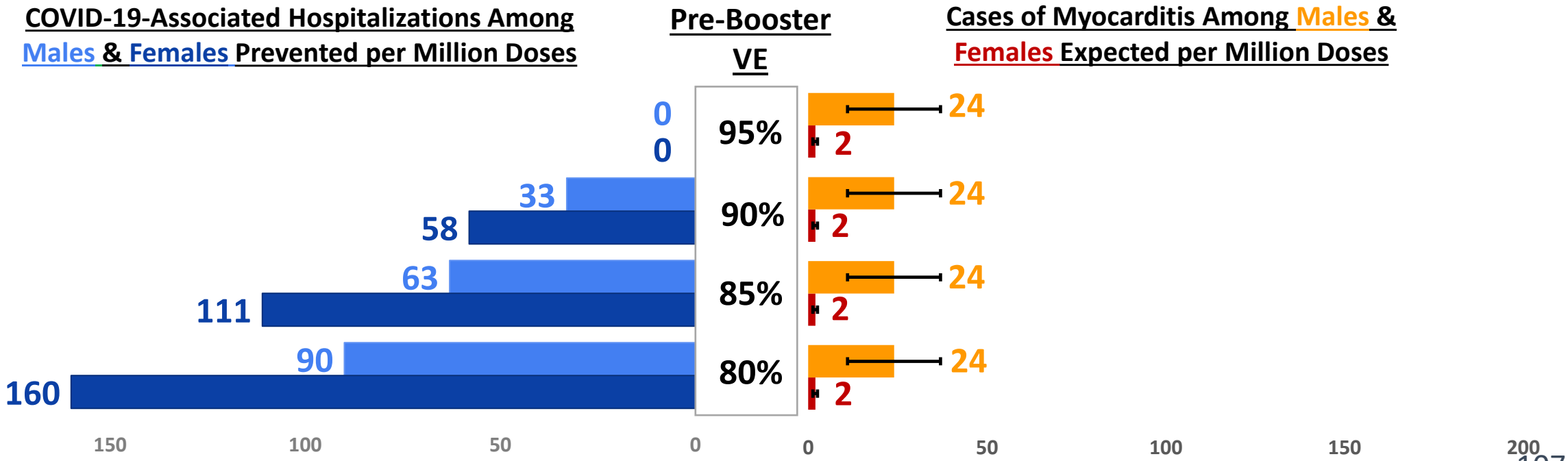


See reference list in later slides

Benefits and risks after Pfizer-BioNTech COVID-19 vaccination for persons aged 18 – 29 years, by sex

For every million doses of vaccine given

Benefit/risk balance among younger population varies by sex, VE after booster dose, rates of myocarditis, and incidence.
As incidence declines, **more uncertainty** around the balance of benefits and risks



[1]https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e1.htm?s_cid=mm7037e1_w.

Evidence Table: Symptomatic laboratory-confirmed COVID-19

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pfizer BioNTech COVID-19 vaccine, 30 mcg, 2 doses 21 days apart	No vaccine	Relative (95% CI)		
Vaccine efficacy against symptomatic COVID-19											
1	RCT	Not serious a	Not serious	Not serious b,c,d	Not serious	None	6/4659 (0.1%)	123/4614 (2.7%)	**RR 0.05** (0.02 to 0.11)	**Type 1**	CRITICAL

a. Risk of bias related to blinding of participants and personnel was present. Although participants and study staff were blinded to intervention assignments, they may have inferred receipt of vaccine or placebo based on reactogenicity. This was deemed unlikely to overestimate efficacy or underestimate risk of serious adverse events, therefore the risk of bias was rated as not serious.

b. The effects noted are from a modified intention to treat analysis with outcomes assessed at least 7 days post booster dose among persons who received a booster dose, and had no evidence of prior SARS-CoV-2 infection. In the all available efficacy population (persons with or without evidence of prior SARS-CoV-2 infection, with outcomes counting from time of booster), there were 15 cases reported among 5,056 persons who received a booster, and 141 cases among 4943 persons who received the placebo, for a relative risk of 0.10 (95% CI: 0.06 to 0.17).

c. The RCT excluded persons with prior COVID-19 diagnosis, pregnant or breastfeeding women, and persons who were immunocompromised. The population included in the RCT may not represent all persons aged >=16 years.

d. Concern for indirectness was noted due to the short duration of observation in the available body of evidence. The booster efficacy observed at a median 2-month follow-up may differ from the efficacy observed with ongoing follow-up.

CI: Confidence interval; **RR:** Risk ratio

Evidence Table: Serious Adverse Events

Certainty assessment							№ of patients		Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparison	Relative (95% CI)		
Serious adverse events											
2	RCT	Not serious [a]	Not serious	Serious[b,c]	Serious[d]	None	16/5055 (0.3%)	24/5020 (0.5%)	**RR 0.66** (0.35 to 1.24)	**Type 3**	CRITICAL

a. Risk of bias related to blinding of participants was present. Although participants and study staff were blinded to intervention assignments, they may have inferred receipt of vaccine or placebo based on reactogenicity. Some reactogenicity outcomes may also have been reported as serious adverse events, and experiences of reactions immediately after vaccination could have influenced recall or reporting of subsequent serious adverse events. This was rated as not serious.
b. The RCT excluded persons with prior COVID-19 diagnosis, pregnant or breastfeeding women, and persons who were immunocompromised. The population included in the RCT may not represent all persons aged ≥16 years.
c. Serious concern of indirectness was noted. The body of evidence does not provide certainty that rare serious adverse events were captured due to the short duration of follow-up and the sample size.
d. Serious concerns of imprecision due to fragility in the estimate was present because there were only 40 events observed from a single RCT

Lymphadenopathy was more common after the 3rd dose than after the 2nd dose

- 135/5055 participants (2.7%) reported lymphadenopathy
  - Typically mild to moderate and located in the axilla or cervical nodes
  - Most occurred 1-3 days post booster and resolved within 1-3 days of onset
  - Frequency higher in younger participants and female participants
- Lymphadenopathy was observed more frequently following the booster dose than after primary series doses (**2.7**% compared to **0.4**%)

Clinical trial data requested by CDC.

Summary

Benefit/risk assessment

- Risks of myocarditis after a 3rd dose of mRNA vaccines is **unknown**
  - Data from Israel suggests risk for Pfizer is between the risks seen for 1st and 2nd dose
- Benefit/risk balance is the most favorable for **adults ≥65 years of age** using current estimates of vaccine effectiveness
- Benefit/risk balance among younger population **varies** by sex, VE after booster dose, rates of myocarditis, and incidence. As incidence declines, more **uncertainty** around the balance of benefits and risks

Survey of fully vaccinated adults (vaccine booster uptake)

- Survey respondents were asked:
  - *"Have you personally received a booster or additional dose of the COVID-19 vaccine after you were already fully vaccinated? When the FDA and the CDC recommend a booster dose of the COVID-19 vaccine for vaccinated people like you, do you think you will…?*

KFF COVID-19 Vaccine Monitor (October 14-24, 2021) KFF COVID-19 Vaccine Monitor: October 2021 | KFF

Vaccine booster hesitancy

- Among those who say they will probably or definitely not get a booster even if the FDA and CDC recommended it for people like them, reasons for not wanting a booster include:
  - feeling they won't need it (14%)
  - believing more research is necessary (13%)
  - saying they have already been vaccinated (9%)
  - lack of trust in the government (8%)

In their own words: What is the main reason why you would not get a booster dose of the COVID-19 vaccine [if the FDA and CDC recommend it for vaccinated people like you]?

"Because they haven't proved it as effective yet and if we really do need it or not." – White man, age 54

"[I'm] confident [in the] first two doses." – Hispanic man, age 21

"Because I got two first dose of the vaccine already and they definitely affected me and my health and there isn't enough information about why I should get this booster shot." – Black man, age 32

"Personal choice not enough evidence or study" – White woman, age 59

"More studies need to be done" – White woman, age 42

"I don't trust anything the government says anymore." – Black man, age 66

KFF COVID-19 Vaccine Monitor (September 13-22, 2021) KFF COVID-19 Vaccine Monitor: September 2021 | KFF

Evidence to Recommendations (EtR) Framework

Policy Question

- Should the recommendations for those who **may receive** a booster dose of Pfizer-BioNTech COVID-19 vaccine be expanded to include all individuals ≥18 years of age ≥6 months after completion of the mRNA primary series under the current Emergency Use Authorization, based on the balance of benefits and risks?

Alternative language for the policy question

Definition of ‘fully vaccinated’

- For public health purposes, people who have completed a primary vaccine series (i.e., 2-dose mRNA vaccine series or a single dose of the Janssen COVID-19 Vaccine [Johnson & Johnson]) are considered fully vaccinated ≥2 weeks after completion of the primary series
- The above definition applies to all people including those recommended to receive an additional single dose due to moderate to severe immunocompromise and those recommended to receive a booster dose

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html

Myocarditis in Israel

Reported after Pfizer-BioNTech COVID-19 vaccine, December 2020-November 15, 2021

	Age (years)	Post-dose 1 Rate per 100,000	Post-dose 2 Rate per 100,000	Post-dose 3 Rate per 100,000	Number of 3rd dose delivered
Females	12-15	0	0.6	0	279
	16-19	0	0.9	0	97,807
	20-24	0.4	2.0	0	141,910
	25-29	0	0.9	0	130,283
	≥30	0.1	0.4	0.1	1,542,142
Males	12-15	0.5	6.9	0	341
	16-19	1.2	16.4	5.4	111,175
	20-24	2.2	10.6	5.0	159,171
	25-29	1.2	8.3	0.7	151,285
	≥30	0.3	1.5	0.9	1,512,135

Rates of myocarditis after a third dose appear to fall **between** rates seen after **dose 1** and **dose 2**

Data provided by Israel MOH